OBSTETRICS AS A DISCIPLINE *

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WHAT does the word " discipline " signify to us ? When I hear it I first conjure up a picture of the Guards going forward calm and unruffled under heavy fire, and I remember what the centurion said: " I am a man set under authority, having under me soldiers, and I say unto one, Go, and he goeth; and to another, Come, and he cometh; and to my servant, do this, and he doeth it ". The first meaning given to it in the *Concise Oxford Dictionary* is " a branch of instruction (archaic) ". It now has become popular in this meaning, with a background of preparation and dedication, so that it amounts almost to a way of life. To the discipline of obstetrics in both senses many general practitioners and many gynæcologists have been subject.

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It has fallen to my lot, in my career as a doctor, to practise obstetrics. It is my firm belief that there is no finer craft in the whole wide field of medicine. I have also practised gynæcology and enjoyed it. But my first love is obstetrics.

Obstetrics presents certain characteristics. Let me first quote John Fairbairn, second president of the college:

" Midwifery is a branch of preventive medicine, because pregnancy, labour and the puerperium are physiological and not pathological states, and the woman at these times is not a sick woman. The whole end and object of midwifery is to maintain the physiological character of these states so as to prevent illness and injury to the woman and secure the birth of a healthy and uninjured child." [3]

When we undertake the care of a maternity patient we are usually dealing with a woman in the bloom of her healthy maturity, joyfully fulfilling her supreme function. At least one poet has seen supreme beauty in this physiological state:

" Three things there are more beautiful
Than any man could wish to see:
The first, it is a full-rigged ship
Sailing with all her sails set free;
The second, when the wind and sun
Are playing in a field of corn;
The third, a woman, young and fair,
Showing her child before it is born."

Fairbairn's statement is undoubtedly correct—our aim is to maintain the physiological character of pregnancy, labour, and the puerperium, and to secure the birth of a healthy and uninjured child. But often, in our present state of knowledge, we cannot do more than keep within bounds complications that are beyond our power to avert completely. By careful antenatal supervision we can almost invariably prevent eclampsia. We cannot prevent pre-eclampsia, though we can usually ensure that it does not become serious. We can sometimes prevent hæmorrhage from placenta prævia, when our attention is attracted by a high presenting part before any bleeding has occurred, and the radiologist makes the diagnosis for us; in most of the cases we can minimise the blood-loss by following the principles of management enunciated by Macafee [6]—that is, we can ensure that the complication does not become serious. The other important point relating to all kinds of hæmorrhage is to be constantly well informed about the blood state by hæmoglobin estimations, and to ensure by suitable treatment that the figure is kept high. A patient with a hæmoglobin of 90% is much fitter to stand loss than one with a figure of 65%. The Macafee regime for placenta prævia is also a valuable contribution to the prevention of prematurity, the chief factor in neonatal mortality. Bender [1] has pointed out that, for patients with twins, rest in bed from the end of the 33rd week significantly reduces the incidence of immaturity. Much potential obstructed labour is preventable by being well informed about the relation of the presenting part to the pelvis during pregnancy. More potential obstructed and difficult labour can be avoided by the correction of malpresentations before labour. The routine careful examination of the whole body, sometimes the first of the patient's life, not infrequently reveals general disease previously undiagnosed—heart-disease, nephritis, phthisis, diabetes, among others—and forewarned is forearmed.

A corollary to the predominance of the normal in antenatal supervision is that we need to be wide awake all the time. For example: because almost every patient in the last month of pregnancy has her baby lying as a vertex, it is easy, if we are not alert, to miss the occasional breech.

Last but not least, the frequent visits to the doctor provide an opportunity for the establishment of the patient's confidence in him. In other words, good antenatal supervision casts out fear. One of the most fear-dispelling statements you can make to her is: "When you are having your baby I shall be there ".

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The psychological problems that are evident throughout medicine are perhaps particularly prominent in obstetrics. The pregnant woman is peculiarly liable to bad suggestion from her fellows, her predecessors, and sometimes alas even from her advisers, who should know better. I often think how very variable is the effect of the parasite on the maternal psyche. At one end of the scale we have a few women who ail from beginning to end of pregnancy, and at the other a large number whose pathognomonic remark is " I never felt better in my life ". A great deal can be done by the wise doctor in helping candidates for the first class to adjust themselves to their state.

There is an analogy between certain aspects of obstetrics and war. For this reason I quote at this point a passage from Lord Montgomery's memoirs:

" No modern Commander-in-Chief can have any success if he fails to understand the human approach to war. Battles are won primarily in the hearts of men; if he loses the battle for the hearts of his men he will achieve little."

Mutatis mutandis this applies to labour. Fairbairn warns us that

" the danger of too much examination is that the woman may think her condition is not physiological but pathological, and hence throughout this part of the work it is essential that the impression given should be that the supervision is merely an exercise of caution, and when everything is normal and straightforward, the assurance should be given that a perfectly natural labour is to be expected. Every individual patient must be treated as a problem in herself."

In all the ways I have mentioned the skill of the doctor can do much to ensure the objects enunciated by

* The Purvis oration for 1958, given before the West Kent Medico-Chirurgical Society on Dec. 12.

Fairbairn, and when they are attained there is a strong feeling of satisfaction, not surpassed by any other professional achievement of which I have knowledge.

There would I think be general agreement that the practice of obstetrics—by which I include care for the woman from booking right through to the postnatal examination—is a hard discipline. At any rate that is the view of many who spend or have spent a large part of their time on it. When the coat-of-arms for the British (now Royal) College of Obstetricians and Gynæcologists was being considered, the first president, William Blair Bell, and the Somerset Herald between them introduced into the arms the crescent moon, to provide "light in the darkness for those whose work continues into the night", and blue and black fields on the shield to indicate day and night. This, as the heraldic description has it, conveys to the mind something that is happening always, day and night. The motto *super ardua*—"over difficulties"—happens to have been taken from Blair Bell's own coat-of-arms, though it is apt both for women labouring of child and also for those who have charge of them. But if the toil is great, the spiritual reward can also be great.

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The most attractive feature of general practice to many is the close personal relationship of the doctor with his patients. This is particularly true in obstetrics, and the relationship is often first established over the birth of a baby. It is for this reason no doubt that obstetrics has been called "the foundation of general practice". In consulting practice the doctor-patient relationship is nearly always a transient one: it is in his obstetric work that the gynæcologist most nearly approaches the general practitioner in this relationship. He sees the patient regularly for some nine months as a rule, helps her to prepare for an outstanding event in her life, and supports her during it. The relationship is a very personal one. I well remember a distinguished obstetrician in my drawingroom some years ago saying that, provided the antenatal care was well done by the doctor, his attendance at the normal labour did not matter. He was fallen on by two of the mothers present, who felt that they had selected their obstetrician with great care, and said that it mattered greatly to them that he should be there during labour and at the birth of the child.

When the patient feels like this, a booked confinement inevitably becomes a great honour, a great responsibility, and a great tie. You cannot let her down by leaving her to a deputy, or, if you are in general practice, to a partner or assistant; and the result is that if you go out to the theatre or away at the weekend you remain within call with a telephone number given; and if the call comes, you go. Like the centurion, you are a man set under authority, the authority of the best professional tradition. I know that this is the view taken by many general practitioners and many consultants, though there are exceptions. Few patients realise fully how much the doctor may give up to be with them on their great occasion.

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There are many emotional crises with which we have to deal. One of the most fascinating puzzles in medicine is prognosis. I still find it quite impossible to be anything like sure which patient will behave with courage during her labour, and which will not. So often one who to all appearances is calm and poised beforehand takes her ordeal very hardly, while frequently the highly strung girl who has been full of worries braces herself and puts up a magnificent performance. Who has not met problems such as the death of the fœtus before labour, sudden disappearance of the fœtal heart during labour, or the birth of an abnormal baby? The unexpectedness of these disasters, our ignorance in failing to anticipate them and our realisation of it, help in at any rate the more modest of us to counterbalance that flattery by which we are so easily persuaded how wonderful we are. They are a challenge to our powers of administering the right comfort for the time being and of inspiring hope for the future.

On one occasion, perhaps fifteen years ago, I was attending a primigravida whose second stage was delayed shortly after I had assured her husband, who was waiting in the nursing-home, that all was well. I stayed in her room while the delay developed, and decided that it was time to apply the forceps. I did this without seeing the husband again. On examining the patient under anæsthesia I found to my surprise that I was dealing with a brow presentation. This I succeeded in flexing, and then the extraction presented no difficulty. Thrilled by my skill and its success I went to tell the husband that both were doing well, and receive my meed of praise. I found a wildly excited gentleman of murderous mien who thought very little of me indeed, and who took a great deal of pacifying. This was a lesson in the importance of the personal touch, not only with the patient, but also with her husband.

May I plead, if it is necessary to plead, that this personal relationship be not abandoned?

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I must say something about the practice of leaving the care of labour to the midwife. This is encouraged in the National Health Service by paying the doctor the same fee whether he attends the delivery or any part of the labour or not. Presumably this arrangement was suggested by somebody who wished to keep the doctor out of the way. Its effect is that in England and Wales only 21% of doctors put in an appearance during labour, whereas in Northern Ireland, where the full fee is not payable without attendance in labour, 81% attend. I cannot myself see how a doctor can be satisfied merely with antenatal and postnatal attendance. During pregnancy he prepares, or should prepare, the patient for her labour, and then when it comes, he is not there—just when she needs him most.

To what can I compare this habit? It is somewhat as though the conductor of the orchestra took all the rehearsals, and then on the night of the concert left the supervision of the performance to a deputy. We have often criticised the local-authority antenatal clinics because their medical officers supervise pregnancy but do not attend labour. Now under the National Health Service many more general practitioners are doing the antenatal care on their own patients, but they often render themselves liable to the very criticism we have levelled at the clinic doctors.

I am, of course, aware that many doctors do attend labour. For instance, Jameson [4] told us at the British Congress of Obstetrics and Gynæcology in Oxford in 1955 that he with one assistant had had the care of over 300 maternity patients in the previous two years, and one or both of them had been present at the confinement of at least 90% of these. This presence is necessary in order to feel that the task has been done completely and well. Apart from the feeling of content that it gives the doctor, there are advantages to the patient. It is much more likely that a needed episiotomy will be done, and that a forceps delivery will be carried out at the right moment, if the doctor is on the spot. Perineal tears needing suture are more likely to be dealt with. The

sentiment that it is quite unnecessary for him to be there, which one hears so often from midwives and their partisans, carries us back a couple of centuries to *Tristram Shandy*, except that poor old Dr. Slop *was* allowed to be in the house, and indeed " to drink a bottle of wine with my father and my Uncle Toby in the back parlour, for which he was to be paid five guineas." Delivery, remember, is still the most important event in the syndrome, not only to the patient and her husband but also to the doctor and the midwife. I doubt whether the photographs of babies which are seen adorning the consulting-rooms of doctors, general and special, are often given to those who did not see them born.

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A favourite quotation of Moynihan's, taken from John Ray's complete collection of English proverbs, published in 1670, stated that the good surgeon should possess an eagle's eye, a lion's heart, a lady's hand. This applies no less to the artist in obstetrics.

Gentleness, like honesty, besides being desirable in itself, is also the best policy. Rough manipulation in trying to perform external cephalic version may stimulate such a defence mechanism in the abdominal wall that turning is impossible, whereas kinder hands often coax the baby round without difficulty. Gentleness is again the supreme quality called for in the use of that remarkable instrument, the obstetric forceps. It has been called both good and bad names, because it can be a power for great good or great harm. McClintock wrote of it in his edition of Smellie's *Midwifery*:

" this noble instrument, which has done more to abridge human suffering and to save human life, than any other instrument in the whole range of surgical appliances. Nay, more, the acquisition of this efficacious resource contributed most influentially to open up a new era in midwifery, by rescuing it from the hands of ignorant female practitioners. The discovery of the forceps, therefore, may fairly be regarded as the most salient and important epoch in the history of obstetrics." [7]

Munro Kerr and Moir have written with equal truth:

" The amount of traction which can be exerted by forceps, especially axis traction forceps, is enormous, because if well applied, the blades grasp the head so exactly. It is this perfection of design which makes the obstetric forceps such a dangerous instrument in the hands of the inexperienced and the aggressive accoucheur, who does not appreciate his own limitations and the limitations of the instrument. We have witnessed an accoucheur with his feet up against the couch, even applied to the buttocks of the patient, exerting all his strength. Occasionally a considerable amount of force has to be employed, although this is seldom justifiable. The instrument is then, as a rule, being used in a wrong manner, or too early, or is unsuitable in the particular circumstances." [8]

Many people quite wrongly associate the forceps with the first five letters of its name. The addition of the PS, or postscript, converts it into what should be regarded as the gentlest instrument. The baby's head, the maternal soft parts, are not structures on which to use force.

Views on the propriety of using forceps have markedly altered during my obstetric lifetime. The substitution of the lower-segment for the classical operation had markedly reduced the risk of cæsarean section before safer anæsthesia, readier resort to blood-transfusion, and the advent of the sulphonamides and antibiotics lowered it still further. The position now is that section is safer not only to the baby but also to the mother than high forceps and many difficult mid forceps. The high-forceps operation has been abandoned almost everywhere for many years, and obstetricians now often prefer section to a mid-forceps operation that is likely to be traumatic. But the incidence of the low-forceps operation, where the head is visible at the vulva, has greatly increased. It is no longer justifiable to wait until the mother is in danger, as shown by exhaustion, acetonuris, or a rising pulse, or until the baby is showing signs of distress, before applying forceps. If progress is slow and the head is low, distress must be anticipated. DeLee [2] introduced the term " prophylactic " forceps, for the operation prevents fœtal asphyxia, intracranial injury and death, maternal exhaustion, and psychological upset that may affect the patient for life. The more frequent use of forceps has been accompanied by a marked drop in the maternal and fœtal mortalities associated with the operation, and has increased the power of the instrument, as McClintock put it, " to abridge human suffering ".

It is time that we began to speak of " masterly interference " as well as " masterly inactivity ", and the same warning applies to both. If you must be inactive, see that your abstinence is an inspired abstinence; if you must interfere see that your intervention is an inspired intervention. It all turns on that quality which has so many opportunities in obstetrics, that combination of intelligence and experience which we call judgment.

* * *

Gentleness is again called for in that manœuvre, or rather sequence of manœuvres, which constitutes perhaps the distilled essence, the supreme accomplishment of obstetric manipulation—by which I mean breech extraction. Also an unruffled mind; or, if the mind is not completely calm, at any rate patience, so that mental disquiet is not translated into violent action. And inflexible resolution, so that, without hurry, progress is made. And finally patience most of all in the delivery of the head, whether you do this with the forceps or your unaided hands.

It is perhaps in breech delivery that the obstetrician most feels the power of life and death in his control. The fact of the living state of the baby is forced on us by feeling directly with our hands its movements, or by feeling or seeing respiratory efforts before it is completely born. We know that if we are too slow, and even more probably if we are too quick, the baby will be stillborn or receive such damage that it will not live long. Some of you may know the story told by Loomis in his book *Consulting Room* [5]:

He was extracting a breech baby, a girl, and on attempting to bring down the second leg he found that the whole of the thigh was missing. He thought rapidly. The mother was an emotional, highly strung woman, and it struck him that the birth of this child would have a terrible effect on her. He pictured the sad and lonely life the child herself would lead, unable to run or play or dance. He realised that it was in his power to deliver the baby stillborn. He had just about decided he must do this when the foot on the good side kicked him, and he felt he could not. The baby was born alive. The effect on the mother was as he expected, and the parents went from one centre to another trying to find someone who could do something for the child. He lost sight of them. Seventeen years later the obstetrician attended a Christmas concert at his hospital, at which a young harpist played with consummate skill. It was the breech baby: she had an artificial limb, she could walk and swim, and was in the view of her mother going to be " one of the world's great harpists ". The important thing was that they were both happy. For many handicapped people there are wonderful compensations, and it is not for the obstetrician to usurp the divine function.

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Six years ago I gave up private practice and became full-time in my chair. It was borne in on me even more forcibly than before, now that I was restricted to hospital practice, how desirable it was that there too there should be, as far as possible, the personal touch. The hospital patient is treated not by an individual but by a team. Each patient should know the names and functions of the people with whom she is brought in contact, and should be brought to realise that they are all on her side, keen that she should remain well, produce a healthy baby, and recover quickly from her confinement.

Many of our patients go through a course of exercises during pregnancy and receive that encouragement which is even more important; there are mothercraft classes and instruction in use of the gas-and-air machine. Every patient is handed a paper giving the names of members of the staff she may meet, with the work each one does. Every few weeks I see a batch of about ten patients who are asked to attend voluntarily and put to me any difficulties or queries they may have, mainly related to medical aspects of their state. This is informal, and I think more satisfactory than formal lecturing. A woman, as Shakespeare might well have said, has not only hands, organs, dimensions, but also senses, affections, passions; and if we are not aware of these, and in a position to take them into consideration, we shall be doing less than our best for her.

It appears that not all hospital doctors realise this, and shortly after writing what I have just said I was handed the report of the Ministry of Health for 1957 in which many of the points I have made are stressed. The report to my mind errs in advising private interviews by the midwife in hospital; these in my judgment should be given by the doctor who takes the ultimate responsibility. In domiciliary practice, too, comfort and advice should be given by the man who takes the responsibility for all the medical problems of the mother's life, not by the midwife who shortly after the baby's birth is no longer concerned with her.

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I have by no means covered all aspects of the discipline of obstetrics; I have spoken of the opportunities it offers for the practice of preventive medicine, touched lightly on the psyche of doctor and patient, emphasised the value of attendance at labour, and said a word or two about antenatal manipulations and the common forms of assisted delivery. I hope that, while saying all this, I have made it clear why the discipline of obstetrics has appealed to me. If I have not, let me finish with a quotation from *Nicholas Nickleby*, which expresses at any rate some of my feelings. Mrs. Kenwigs had just produced her sixth, and Mr. Lumbey, the doctor, comments to Mr. Kenwigs: " ' It's the finest boy I ever saw in all my life. . . . I never saw such a baby '. It is a pleasant thing to reflect upon and furnishes a complete answer to those who contend for the gradual degeneration of the human species, that every baby born into the world is a finer one than the last. ' I ne-ever saw such a baby ', said Mr. Lumbey the doctor."

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THIRST AND POLYURIA

WITH A NOTE ON THE EFFECTS OF POTASSIUM DEFICIENCY AND CALCIUM EXCESS*

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IN the normal person thirst is associated with oliguria; thirst with polyuria is abnormal. The relation of thirst to polyuria has been the subject of much discussion (Tournay 1946), particularly in the syndrome of diabetes insipidus; but the early view that abnormal thirst might be the cause of the polyuria (Bailey and Bremer 1921, Camus and Roussy 1922, Richter 1930) suffered an eclipse when the role of the antidiuretic hormone (A.D.H.) came to be recognised. Yet a pathological thirst can be the cause of polyuria, and there are also instances where thirst and polyuria are associated but are independent of each other.

Thirst

Thirst is the sensation which arouses a desire for water. The information which this sensation provides is vital, for without it deficits of water go unheeded. A.D.H. minimises losses of water: thirst ensures that they are replaced.

The Origins of Thirst

A sensation may arise peripherally or centrally; attempts to localise the origin of thirst peripherally have so far failed. The theory that a dry mouth accounts for thirst was put forward by Cannon (1918). But this is not a complete explanation, since water deprivation produces thirst long before the mouth becomes dry. Moreover, thirst is not relieved simply by wetting the mouth (Allison and Critchley 1943); the climber derives little comfort from sucking snow, and an increase in the salivary flow (induced by sucking a pebble or by the injection of pilocarpine) does not abolish the desire for water (Adolph and Wills 1947). Nor does a dry mouth necessarily make people thirsty; the discomfort caused by atropine is seldom described as thirst, and rarely promotes drinking. Thirst is not abolished by excision of the pharynx, œsophagus, or stomach; therefore it cannot arise in these organs.

There is now both experimental and clinical evidence that thirst arises from a thirst " centre ". Work on goats provides the best experimental evidence (Andersson 1957).

When Andersson and McCann applied an electrical stimulus to a certain area in the hypothalamus near the supraoptic nucleus, the goats drank enormous amounts of water, and some of them diluted their body fluids so much that they lysed their own red blood-cells. If the same area was destroyed the goats would not drink even when they were dying from water depletion. Since some, but not all, of the goats in which thirst was abolished also developed diabetes insipidus, the thirst centre must be closely related to the hypothalamic centre for antidiuresis.

The clinical evidence for the existence of a similar thirst centre in man will be described below.

Stimulation of Thirst

The centres for thirst and antidiuresis can be stimulated in similar ways. The most obvious common stimulus

* Based on a lecture given by P. F. at the Postgraduate Medical School of London on March 10, 1958.

is a deficit of water; this reduces the volume of the body fluids and increases their tonicity.

A rise in tonicity has long been held to be the stimulus for thirst (Mayer 1900, Leschke 1918). But thirst can be stimulated by the injection of hypertonic saline and not by the injection of urea (Gilman 1937), though both solutions raise the tonicity of the body fluids. This might be because sodium chloride does not enter the cells, and injection of saline therefore shrinks the cells, whereas urea, which diffuses across the cell membrane, does not. This suggests that the shrinkage of the cells, and not the hypertonicity, is the effective stimulus; and it seems likely that it is the shrinkage of specialised receptor-cells in the hypothalamus that initiates both thirst and antidiuresis.

Wolf (1950) has calculated that a rise of a little over 1% in the osmotic pressure of the body fluids stimulates thirst, and Verney (1957) found that a similar rise stimulates the liberation of A.D.H. This rise also reduces the flow of saliva (Holmes and Gregersen 1947); thus the central effect on thirst is reinforced by dryness in the mouth.

In the healthy person thirst and the liberation of A.D.H. together maintain the tonicity of the body fluids within narrow limits. Some patients have an abnormally low level of sodium in the extracellular fluid without showing any of the symptoms of sodium deficiency (Leaf and Mamby 1952). Attempts to raise the level of sodium by infusion of saline lead to immediate antidiuresis and thirst, which cause the low sodium level to be maintained (Elkinton 1956). In such patients the low tonicity of the extracellular fluid must reflect a fall in the osmotic pressure of the cellular fluid, otherwise the cells would swell, causing symptoms of water intoxication.

Thirst accompanies a number of clinical states associated with a fall in the volume of the extracellular fluids without any change in tonicity (Strauss 1958).

Thirst may be the first symptom of a gastrointestinal hæmorrhage, though not usually when the loss of blood is small (Holmes and Montgomery 1951). Thirst often follows the removal of ascitic fluid (Nelson et al. 1951); and it may precede the appearance of œdema in cardiac failure or in the nephrotic syndrome.

Experimentally, the withdrawal of extracellular fluid leads to an increased intake of water (Holmes and Cizek 1951, Cizek et al. 1951). The removal of extracellular fluid probably reduces the volume of circulating blood. There are known to be receptors in the left auricle which are sensitive to changes in pressure. The impulses they initiate may control the volume of body fluid by stimulating the release of A.D.H. (Henry and Pearce 1956). Possibly these impulses also stimulate thirst. As an alternative mechanism, a fall in the volume of circulating blood may produce a release of aldosterone (Bartter et al. 1958), and some observations suggest that aldosterone can itself stimulate the thirst centre (Chalmers et al. 1956, Stanbury et al. 1958).

There remain instances of thirst which are not explained by changes in tonicity or volume, and which may be the result of chemical changes; as these changes can also produce polyuria, they will be discussed later.

Failure of the Thirst Mechanism

The physiologist recognises that thirst may be inhibited by muscular activity (Adolph and Wills 1947). Distension of the stomach inhibits thirst (Towbin 1949), and this explains why man may not always immediately replace a large deficit of water; when acclimatised to life in the desert he acquires the faculty of drinking more at one time (Adolph 1950). Fluid depletion from gastrointestinal losses sometimes fails to provoke thirst.

Nadal et al. (1941) aspirated the jejunal secretions of two normal men who were allowed to drink water; these men did not become thirsty, although their loss of body fluid was sufficient to cause peripheral circulatory failure. We do not know why their thirst failed.

The most obvious examples of a failure of the thirst mechanism are those patients who, in spite of a high plasma-sodium, do not drink. In elderly and very ill people this may simply be the result of mental confusion or apathy. When dehydration is once established it may itself so impair mental function that the desire for water is lost (Brown 1947). For this reason it may be difficult to persuade some patients to drink when they have a severe water deficiency, although they may demand water as soon as their deficit has been partially corrected.

Lesions of the thirst centre and its tracts must account for many of the cases described as cerebral hypernatræmia. Amongst the recorded cases of diabetes insipidus there are some patients who had an unnaturally high plasma-sodium level without suffering thirst (Peters 1948, Leaf and Mamby 1952, Engström and Liebman 1953, Fourman and Leeson 1958). In these examples the lesion responsible for the diabetes insipidus was presumably in the hypothalamus, and had also destroyed the thirst centre. But in the usual form of diabetes insipidus, produced by destruction of the posterior-pituitary gland and the pituitary stalk, thirst arises after polyuria, and the resulting large intake of water prevents the serum-sodium from rising above normal (Holmes and Gregersen 1948).

Primary Polydipsia

Polydipsia can be the cause of polyuria (Nothnagel 1881, Lhermitte 1946, Alajouanine and Thurel 1946). Such a polydipsia is often hysterical or obsessional; but it may be the result of a local lesion stimulating the thirst centre.

Kourilsky et al. (1942) described a young woman who fractured the base of her skull and later had headaches, anosmia, hemianopia, optic atrophy, and above all an overwhelming thirst. Three years after her injury, an operation under local anæsthesia revealed an arachnoid cyst, extending from the sylvian fissure to the optic chiasma, which was pressing on the hypothalamus and pituitary stalk. During the operation she continued to complain of thirst; but the moment the cyst was drained, she exclaimed " I have lost my thirst ". It never returned.

There have also been instances where thirst began during an operation on the base of the brain (Alajouanine et al. 1934).

Some patients with polydipsia apparently of psychological origin have later developed menstrual disturbances, obesity, and evidence of lesions in the upper part of the brain-stem. This suggests that their initial polydipsia might have been caused by a cerebral lesion rather than by a compulsive psychosis.

We have observed a man with thirst of sudden onset whose symptom was replaced immediately after an air-encephalogram by one of revulsion for water. His plasma-osmolality was 275 milliosmoles per litre when he was thirsty, and 280 when he was refusing to drink.

In such cases, there is no simple way of distinguishing " functional " polydipsia from pathological thirst of organic origin, though other symptoms may sometimes point to the correct diagnosis. A strong emotion may produce thirst. This could be an effect of the release of adrenaline (Holmes and Montgomery 1953), or of a nervous stimulus to the thirst centre.

Polyuria

Polyuria is the excretion of large volumes of urine.

In the normal person its cause may be: (1) the adminis-

tration of too much water, or (2) the need to excrete an excess of solute. An excess of water produces urine which is more dilute than the plasma; an excess of solute produces urine which is either of the same concentration as the plasma or slightly more concentrated.

The fluid entering the renal tubules from the glomeruli is isotonic with the plasma. In the proximal tubules the tonicity does not change, but the volume is normally reduced by 85% through the absorption of sodium and water. In the distal tubules the fluid always becomes hypotonic through the reabsorption of sodium (Wirz 1956). In order to make the final urine hypertonic, water must be reabsorbed either in the last part of the distal tubules or in the collecting tubules. This process normally requires A.D.H.; without it the urine is hypotonic, unless a very small volume of glomerular filtrate is delivered to normal tubules, when hypertonic urine can be formed without A.D.H. (del Greco and de Wardener 1956, Berliner and Davidson 1957).

Only a limited amount of water can be removed from the tubular fluid during the final concentrating process; consequently as the flow of tubular fluid increases the maximum concentration of the urine falls. Thus, in an osmotic diuresis, the proportion of the glomerular filtrate reabsorbed by the proximal tubules is reduced, more fluid is delivered to the distal tubules, and the concentration of the urine diminishes. But, in the presence of A.D.H., the urinary concentration does not become less than that of the plasma.

In disease, polyuria may represent an osmotic diuresis (with an isotonic or slightly hypertonic urine), or a water diuresis (with a hypotonic urine) (Welt 1956). An osmotic diuresis may account for the polyuria in renal failure with uræmia (Platt 1952), and in diabetes mellitus. An abnormal water diuresis (diabetes insipidus) may arise for two reasons: (1) because the pituitary gland fails to release A.D.H.—pituitary diabetes insipidus—or (2) because the renal tubules fail to respond to A.D.H.—renal diabetes insipidus. Vasopressin cures the first condition but not the second.

Renal diabetes insipidus may be the sole manifestation of a genetic disorder (Williams and Henry 1947), or it may accompany other inborn defects of tubular function as in the Fanconi syndrome (Bickel et al. 1952, Stanbury 1958). It may appear in various other conditions, such as obstructive lesions of the renal tract and multiple myelomatosis (Roussak and Oleesky 1954).

Finally, sustained drinking and the consequent excretion of large amounts of water may itself diminish the ability of the kidneys to reabsorb water. After drinking 10 litres of water daily for ten days, de Wardener and Herxheimer (1957) found that they could not conserve water normally when deprived of it, and their response to vasopressin also was impaired. Primary polydipsia may thus lead to a transient renal diabetes insipidus.

Potassium Deficiency and Calcium Excess

Congenital and acquired defects of the renal tubules may result in wastage of potassium as well as water. Potassium deficiency itself impairs the tubular reabsorption of water (Brokaw 1953, Dustan et al. 1956, Relman and Schwartz 1956), presumably by producing lesions of the collecting ducts (Oliver et al. 1957).

Potassium and calcium are in many ways physiological antagonists; an excess of calcium, like a deficiency of potassium, can produce renal diabetes insipidus (Cohen et al. 1957, Epstein et al. 1958). Polydipsia and polyuria are occasionally the first and most prominent symptoms of hyperparathyroidism; they must result from the hypercalcæmia rather than from the excess of parathyroid hormone, since the same symptoms may appear with hypercalcæmia from other causes, such as osteolytic infiltration of bone, the milk-and-alkali syndrome, and vitamin-D intoxication. The polyuria of potassium deficiency or calcium excess rapidly disappears when the biochemical disturbance is corrected.

In these examples of polyuria of renal or metabolic origin, one might assume that the polyuria would account for the thirst of which these patients also complain. We wish to suggest, however, that the thirst may not depend on the polyuria, but may be the result of a chemical stimulus to the thirst centre. The thirst is not closely related to the loss of water, nor is it always relieved by drinking.

In one of the first experimental deficiencies of potassium studied in man, drinking 8 litres of water a day did not relieve the thirst (Fourman 1954). Potassium-deficient rats increased their water-intake before they had any detectable impairment of urine-concentrating power (Hollander et al. 1957).

In hypercalcæmia there may be thirst without polyuria. We have studied a woman of 64 with hyperparathyroidism who had had undue thirst for eight months. For some time it was the only symptom, but during the last three months she also noticed nocturia and pains in the limbs, and she lost weight. She had no apparent bone disease or renal calcification, but her renal function was poor; the blood-urea was 71 mg. per 100 ml., and the inulin clearance was 35·5 ml. per min. But she did not have polyuria, and despite her complaint of thirst she did not drink a great deal. The daily urine-volume was 1200–1400 ml., and the maximum urine concentration was 654 milliosmoles per litre (specific gravity 1014). The sodium level and osmolality of the plasma were normal; the serum-calcium ranged from 15 to 20 mg. per 100 ml. Six hours after the removal of a parathyroid adenoma the serum-calcium had fallen to 13·5 mg. per 100 ml., and her thirst had vanished.

Evidence such as this has led us to conclude that potassium deficiency and calcium excess may sometimes directly stimulate the thirst centre, and that the thirst in these disorders does not necessarily depend on any associated polyuria.

In patients with uræmia or diabetic acidosis, thirst is often the result of water loss, but it may sometimes represent a direct biochemical effect on the thirst centre. In prolonged renal failure, thirst may persist after the dehydration has been corrected; in acute renal failure, thirst may be a prominent symptom though there is no renal water loss, and it may even persist when the patient has been given too much water. The following data are from three patients who had anuria and were thirsty:

	Patient 1	Patient 2	Patient 3
Sodium (mEq. per litre of plasma) ..	130·0	136·0	137·0
Potassium (mEq. per litre of plasma) ..	4·6	4·4	5·4
CO_2-combining power (mEq. per litre of plasma)	14·0	24·0	25·0
Chloride (mEq. per litre of plasma) ..	81·0	103·0	84·0
Urea (mg. per 100 ml.)	320·0	174·0	292·0

While in patient 1 thirst could have been due to acidosis (the possibility has not been investigated), patient 2 was not acidotic. When patient 3 was extremely thirsty she had retained a large volume of water, she was œdematous, and her tongue was swollen. Although the exact cause of thirst in these patients is not known a chemical stimulus to the thirst centre seems likely.

Summary

The antidiuretic hormone reduces renal loss of water to a minimum; thirst ensures that losses are replaced.

Both mechanisms are controlled by adjacent centres in the hypothalamus, and these can be stimulated in similar ways—e.g., by a deficit of water, or by a rise in the tonicity of the extracellular fluid. Polyuria may represent the failure of antidiuresis. Usually this loss of water stimulates thirst; thus the intake of water is increased, and dehydration is avoided. Occasionally a lesion destroys both centres; without thirst the loss of water is not replaced, and dehydration rapidly ensues.

Polyuria is sometimes the result of excessive drinking. This may be caused by a psychosis, or by pathological stimulation of the thirst centre.

Potassium deficiency or calcium excess can cause both thirst and polyuria. We think that in these conditions the thirst does not depend on the polyuria, but is produced by a direct biochemical stimulus to the thirst centre. Since the thirst of uræmia appears to be unrelated to the state of hydration, it also may be stimulated by some alteration in the chemical composition of the body fluids.

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THROMBOCYTOPENIA DURING CHLOROTHIAZIDE TREATMENT

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IN this paper we report six cases in which thrombocytopenia developed during treatment with chlorothiazide. Three of them also had a purpuric rash. A case of thrombocytopenia and agranulocytosis following treatment with chlorothiazide has lately been recorded by Zuckerman and Chazan (1958).

To confirm that chlorothiazide was the cause, test doses were given and in-vitro tests were made in two of our patients, and patch tests were performed in three.

The in-vitro tests were: (1) inhibition of clot retraction, (2) immune-precipitate formation, and (3) platelet agglutination and lysis. The Ackroyd (1949, 1952) technique was used for these tests. In addition platelet agglutination was studied on stained blood-films by the method of Hoigné et al. (1954). Chlorothiazide was always added in a concentration of 0·21% in the in-vitro tests. The patients' blood without chlorothiazide added, and blood from two healthy blood-donors, served as controls. All controls were tested at the same time as the in-vitro tests with chlorothiazide were made.

Patch tests with chlorothiazide were performed using a saturated solution in propylene glycol. Pure propylene glycol served as control.

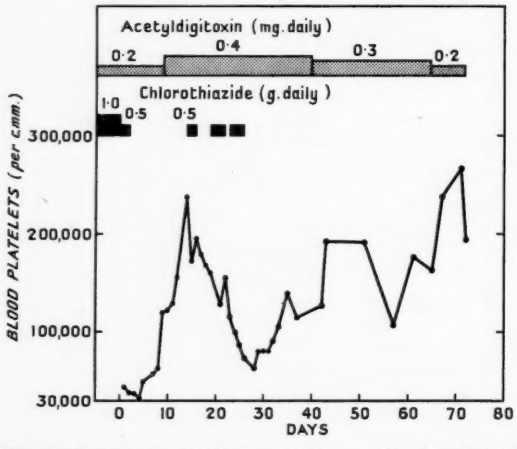
Platelet-counts were made by a technique modified from Kristenson (1924).

Case-reports

Case 1.—A woman, aged 54, had hypertensive cardiovascular disease with heart-failure. She was given chlorothiazide 1 g. daily as the only treatment in order to study its effect on the blood-pressure. On routine examination of her blood, before the drug was given, the platelet-count was 228,000 per c.mm. 22 days later a purpuric rash appeared, and the platelet-count in the peripheral blood was only 19,000 per c.mm. Chlorothiazide therapy was stopped, and for the next 3 days the platelet-count was never more than 35,000. On the 4th day the count was 75,000. 8 days later the rash was no longer visible and she had a normal platelet-count (236,000 per c.mm.). No other toxic reactions of the peripheral blood-cells were observed, and bone-marrow examination after recovery revealed no abnormality. A patch test with chlorothiazide was negative and caused no significant decrease of her platelet-count.

This patient's course was typical of a drug-induced thrombocytopenia, and the only possible drug was chlorothiazide.

Case 2.—A woman of 51 had mitral stenosis and right-sided heart-failure. During therapy with chlorothiazide she had repeated platelet-counts below 35,000 per c.mm. When thrombocytopenia appeared, she was taking chlorothiazide, acetyldigitoxin, and quinidine. When the chlorothiazide and quinidine therapy was stopped, but acetyldigitoxin was still given, the number of platelets quickly became normal. When the platelet-count was stabilised she was again given chlorothiazide as a provocative test, and again the number of circulating platelets fell rapidly. When chlorothiazide was withdrawn the platelet-count increased (see figure). The in-vitro tests on this patient's blood, when she had regained a normal platelet-count, showed that addition of chlorothiazide caused an obvious platelet lysis, platelet agglutination, and a very weak immune-precipitate formation. Clot retraction after the addition of



The platelet-count in case 2 during treatment with chlorothiazide and acetyldigitoxin.

chlorothiazide did not differ significantly from the controls, and a patch test was negative.

During chlorothiazide therapy, when there was thrombocytopenia, she had an intestinal hæmorrhage; she developed also a purpuric rash but this was not quite simultaneous with the low platelet-count.

This case, too, was typical of a drug-induced thrombocytopenia. But besides chlorothiazide she had had other drugs known to cause thrombocytopenia. A test dose of chlorothiazide given without changing the acetyldigitoxin therapy and without giving quinidine indicated strongly that chlorothiazide was the drug which caused the thrombocytopenia. But it is impossible to exclude interference between chlorothiazide and acetyldigitoxin as the cause of thrombocytopenia. In-vitro tests with chlorothiazide were, except for platelet lysis, amazingly weak.

Case 3.—A man of 84 had hypertensive cardiovascular disease and heart-failure. During treatment with chlorothiazide and chloramphenicol thrombocytopenia appeared, and within 2 weeks the platelet-count dropped from 192,000 per c.mm. to 26,000. Repeated counts during the next week were below 40,000 although therapy with both drugs was stopped immediately after the decrease in circulating platelets was noted. On the 7th day the platelet-count started to increase; 3 days later it was 140,000 per c.mm., and 7 days later the count was about 200,000. He was then given chloramphenicol 1 g. daily for 2 days without any drop in his platelet-count. All other formed elements in the blood were normal throughout. 5 months later in-vitro and in-vivo tests were made. After the addition of chlorothiazide, platelet agglutination and clot retraction became positive. No lysis of the platelets and no immune-precipitate formation was observed. Patch testing with chlorothiazide gave a blister and palpable infiltration, but there was no change in colour and no skin bleeding; the control test was negative. He had repeated test doses of chlorothiazide (up to 1 g. daily) without any significant change in the platelet-count. Even when he was given chlorothiazide 1 g. and chloramphenicol 0·5 g. for 2 days the platelet-count did not fall significantly.

Since the test doses in this case did not affect the platelet-count we cannot say that chlorothiazide alone was the cause of the thrombocytopenia. The clinical course suggested a typical drug complication, but one cannot be sure whether it was caused by chloramphenicol alone or by both drugs together. However, the toxic reaction of chloramphenicol has been described as marrow aplasia and not as isolated thrombocytopenia (Garrod 1958), and the positive in-vitro tests show that chlorothiazide was involved in causing the thrombocytopenia. This patient had no purpuric rash. Why the test doses had no effect, although the in-vitro tests for chlorothiazide were positive, cannot be explained. It may be that the test doses were too small or the time for exposure too short for the sensitive mechanism to start.

The other three cases were less definite:

A woman, aged 63, with mild diabetes and with ascites containing neoplastic cells, was given chlorothiazide for 2 months. She was then taken into hospital and found to have a platelet-count of 21,000 per c.mm. After the chlorothiazide had been stopped, and without changing her other treatment, the platelet-count increased; but it did not become normal until 2 months later.

A woman of 48 with mitral stenosis and right-sided heart-failure developed a purpuric rash and hæmaturia during therapy with digitoxin and chlorothiazide. Her platelet-count was then 63,000 per c.mm. She had previously been treated with chloramphenicol also. A week after the chlorothiazide was stopped (the digitoxin still being continued) the hæmaturia ceased and the rash disappeared. She died 3 weeks later, and her platelet-count was still not more than 70,000 per c.mm.

A woman, aged 76, with cardiovascular disease and heart-failure was treated with lanatoside C (' Cedilanid ') and chlorothiazide for 2 months. After that time repeated platelet-counts were around 90,000 per c.mm. When chlorothiazide was stopped the platelet-count became normal within 2 weeks.

Summary and Conclusions

Six cases are described in which thrombocytopenia appeared during chlorothiazide therapy. In two of them there was a direct connection between this drug and the thrombocytopenia, and a third showed positive in-vitro tests for chlorothiazide.

Chlorothiazide was used in this clinic in about 400 cases last year, which indicates that a decrease in circulating platelets may appear in more than 1%.

In all cases the thrombocytopenia was the only toxic manifestation of chlorothiazide in the bone-marrow. The reaction was usually brief, and the platelet-count returned to normal as soon as chlorothiazide was withdrawn.

These observations indicate the desirability of doing a blood-count when chlorothiazide is given to old and debilitated patients, or when it is combined with other drugs that may have a depressing effect on the hæmopoietic system.

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Addendum

Since this paper was written three further articles have been published describing four cases in which there was thrombocytopenia or purpura during treatment with chlorothiazide:

Dinon, L. R., Kim, Y. S., Veer, J. B. V. *Amer. J. med. Sci.* 1958, **236**, 533.
Holboth, N., Thomsen, K., Hansen, P. F., Haagensen, N., Opresnik, J. *Ugeskr. Læg.* 1958, **120**, 1585.
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EMOTIONAL STATE AND ENERGY EXPENDITURE

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EUTHYROID " nervous " subjects are generally believed to show a tendency towards high basal metabolic rates (B.M.R.S) (Means 1937). Estimation under conditions of induced sleep has been recommended (Fraser and Nordin 1955) to avoid diagnostic errors due to emotional upset. The characteristics of nervousness or emotional upset, however, are not defined in published reports, nor have adequate attempts to measure the influence of this factor on the basal metabolic rate been reported. The problem is further complicated by the lack of general agreement regarding the limits of normality in metabolic rate (Booyens and McCance 1957).

Changes in oxygen consumption during emotional responses to extraneous stimuli have been investigated by Landis (1925) who concluded that " emotional disturbance, per se, does not lead to changes in the metabolic rate which are always in the same direction or the same magnitude." On the other hand, Schou (1937) and Finesinger (1939) reported that unpleasant experiences were commonly associated with a small increase in oxygen consumption. These workers were, however, concerned with response to extrinsic stimuli, which, of course, do not operate in clinical measurement of the B.M.R.

We proposed to investigate the strength of the association between emotional state and oxygen requirements in the lying, sitting, and standing positions.

Material and Methods

Thirty-two patients and ten control subjects were tested. The patients were consecutive admissions to the professorial unit at the Maudsley Hospital, except a few who were untestable or had physical disease. They were examined within a few days of admission to hospital, before treatment had been begun. No significant medication was being administered to them. Their serum-protein-bound-iodine values were all within the normal range. Control subjects were persons on the staff of the Institute of Psychiatry.

The psychological state, which varied from practically normal, as in case 20 (an alcoholic admitted for treatment of long-standing addiction), to very severe delusional fear (as in case 13, who had schizoaffective disorder), was assessed in respect of eight symptoms (depression, euphoria, apathy, apprehension, motor excitement, motor retardation, pressure of talk, and mutism), each on a four-point scale. We hoped thus to include essential features which indicate emotional disturbance, of whatever kind, and are readily observable. Two independent ratings were made—one immediately before testing, by the psychiatrist clinically responsible for the patient, the other during the test procedure. It was postulated that, in each of the three positions, the more disturbed patients would exhibit higher energy expenditure than the controls. The latter were rated once only, for manifest emotional state during the actual testing; in them the highest score was 2 (in subject B).

We followed closely the testing procedure of Booyens and McCance (1957). Respiratory volume was measured, and expired air collected using the integrating motor pneumotachograph devised by Wolff (1958). Gas analyses were made with the Scholander (1947) apparatus. A more detailed account of the method and of additional observations (electrical skin resistance, body-build measures, pulse-rate, respiratory rate, serum-protein-bound-iodine) will be reported elsewhere.

Results

The results are shown in the accompanying table:

In the lying position the mean values for patients and controls are not different—97·2% and 98·4% respectively. These values are lower than that reported by Booyens and McCance (1957), which was 103% (recalculated, for purposes of comparison, as a percentage of Robertson and Reid [1952] expected mean). Our controls (79–114%) fall well within the Booyens and McCance (1957) distribution (73–128%). The patients have a somewhat wider range of values (66–126%). They have been divided into two groups of approximately equal size—viz., those with high psychological abnormality as expressed by the aggregate rating score, and those with low scores; their respective means for this position are 97·5% and 97·2%. The distributions for these two groups have been compared in fig. 1.

In the sitting position, mean values for the subjects of Booyens and McCance (1957), our controls, and the patients are 116·7%, 109·0%, and 111·3% respectively. The mean for the more disturbed patients is 112·9%, for the less disturbed 110·7%. The range of caloric cost for

DATA ON 32 PATIENTS AND 10 CONTROLS

Case no.	Age (yr.)	Sex	Surface area (sq. m.)	Expenditure of calories (per sq. m. per hr.) (% of Robertson and Reid mean)			Aggregate psychological score
				Lying	Sitting	Standing	
Patients:							
1	20	F	1·58	82	..	..	5
2	22	F	1·58	82	106	111	9
3	24	M	1·61	76	117	95	17
4	24	F	1·52	119	108	..	8
5	24	F	1·39	110	..	126	4
6	25	M	1·89	66	90	82	15
7	27	F	1·45	96	108	104	9
8	28	F	1·39	123	132	180	18
9	29	M	1·67	84	89	157	17
10	30	F	1·74	106	..	..	15
11	31	F	1·64	99	112	122	9
12	32	M	1·82	103	88	128	6
13	34	M	1·87	121	151	129	18
14	35	F	1·56	100	110	121	3
15	36	M	1·87	70	86	87	2
16	36	M	1·77	86	101	83	10
17	37	F	1·39	89	101	91	4
18	38	M	1·87	102	125	119	13
19	38	M	1·68	120	179	168	4
20	38	M	2·01	67	79	90	1
21	38	M	1·78	101	113	131	10
22	43	F	1·55	110	144	151	3
23	46	M	1·89	91	112	148	8
24	55	F	1·48	126	102	92	11
25	52	F	1·39	124	137	133	6
26	53	F	1·56	91	101	94	2
27	53	M	1·88	88	105	108	4
28	55	M	1·86	86	99	137	8
29	55	F	1·36	98	114	108	5
30	57	F	1·76	90	97	87	5
31	58	F	1·43	107	121	82	15
32	69	F	1·44	97	102	144	7
Means	37·9	..	..	97·2	111·3	117·5	8·6
Controls:							
A	22	F	1·74	86	76	101	..
B	26	F	1·68	107	125	138	..
C	30	M	1·94	114	125	124	..
D	30	M	1·87	97	106	119	..
E	32	F	1·64	79	85	88	..
F	35	M	1·86	97	102	126	..
G	36	M	1·75	114	134	146	..
H	37	M	1·80	96	101	106	..
I	44	F	1·79	109	132	170	..
J	45	F	1·45	85	104	111	..
Means	33·7	..	..	98·4	109·0	122·9	..
Booyens and McCance: means	26·9	..	..	103·0	116·7	129·7	..

* R. S. McLaughlin Foundation travelling fellow.

† Aided by a grant from the Ford Foundation.

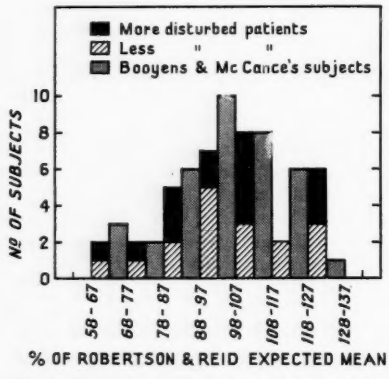

Fig. 1—Energy expenditure in the lying position.

this position is very wide, individual differences being as great for the normals as for the patients. The mean increments are similar.

In the standing position the mean values are 129·7% for the subjects of Booyens and McCance (1957), 122·9% for our controls, and 117·5% for the patients tested; the patients with a high score of psychological symptoms have a mean of 113·7%, those with a low score 122·3%. Mean values for our patients considered as a total group and for our controls are consistently about 7% less than those of Booyens and McCance (1957): this constant discrepancy (which is evident in all three positions) is probably due to the different technique used for the determination of respiratory volume. The distribution of scores among the normals when standing is, however, different from that in the patient group: whereas in normals the cost of standing is higher than that of sitting, many of the patients (about half the group) have a lower oxygen utilisation when standing than when sitting (fig. 2). This finding is more closely related to certain individual symptoms than to the aggregate psychological score, as will be shown in a subsequent paper.

Discussion

The rate of oxygen consumption by these patients when in the lying position is of the same order as in the normal series of Booyens and McCance (1957): the means, corrected for technical variation, are very similar, and the distribution of values in the patients is only slightly wider than in the normals. The increment or decrement

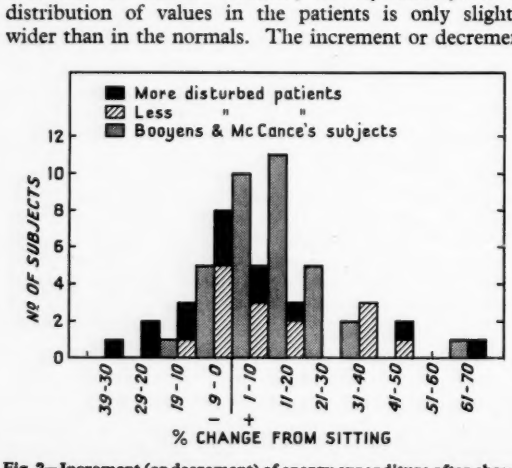

Fig. 2—Increment (or decrement) of energy expenditure after changing to the standing position.

in oxygen utilisation when changing from the sitting to the standing position was much different in the patient group from the normals. The most striking finding was the absence of observed relationship between emotional state and rate of oxygen consumption. A person with very high (or very low) score of psychological disturbance could present with either high or low values. This confirms the observation of Segal et al. (1928) that, in the absence of thyrotoxicosis, emotion does not increase the metabolic rate.

There were no observable differences between the groups in the mean cost of sitting. The wide range of individual energy expenditure is not dissimilar between normals and patients, or between those with high and those with low scores of emotional disturbance.

The mean oxygen utilisation in the standing period was less for the patients than for the controls (122·9% compared with 117·5%). This apparently small difference masks greater disparity between the highly disturbed group (two-thirds of whom showed fall in oxygen uptake from their sitting value) and the less disturbed group (who behaved like the normals). Lower uptake when standing is not restricted to the patients, however, for it was recorded in five cases in Booyens and McCance's (1957) series, though to a minor degree (subjects 8, 17, 20, 30, and 33). This may be related to the finding of Cohen et al. (1946) that during strenuous exercise patients with neurocirculatory asthenia utilised less oxygen than normal persons. Though our patients were not subjected to gross physical effort, the unfamiliar and lengthy testing procedure may have been sufficiently stressful to induce this form of response to even slight physical effort.

Our subjects were inpatients in a psychiatric unit whose symptoms of disturbed emotional state were similar to those observable in " nervous " persons in any medical department. The observations on their oxygen metabolism might, therefore, be applied to emotionally disturbed persons in other settings, and are not in accordance with the belief that emotional disturbance commonly increases the metabolic rate.

Summary

Energy expenditure was studied in thirty-two psychiatric patients and ten healthy subjects in the lying, sitting, and standing positions. The emotional state of the patients and normal subjects was rated at the time of testing. Results in the patients were compared with those of the controls and of another reported series of normal subjects.

The mean oxygen consumption of the patients was not different from that of normal subjects in the lying and sitting positions, but was less in the standing position.

The level of oxygen consumption in the lying and sitting positions was not related to the degree of emotional disturbance, but many of the more disturbed patients showed a decrement in oxygen use on standing up.

In this group of patients, emotional disturbance was not associated with increased oxygen consumption.

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HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE) AND JUVENILE CIRRHOSIS IN THE SAME FAMILY

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IN recent years several cases of hepatolenticular degeneration (Wilson's disease) have been described in which liver dysfunction dominated the clinical picture with few or no signs of involvement of the central nervous system. In such cases the diagnosis usually rests on biochemical or necropsy evidence, but sometimes only on a positive family history (Chalmers et al. 1957). That such a family history needs to be interpreted with caution will be evident from the following report.

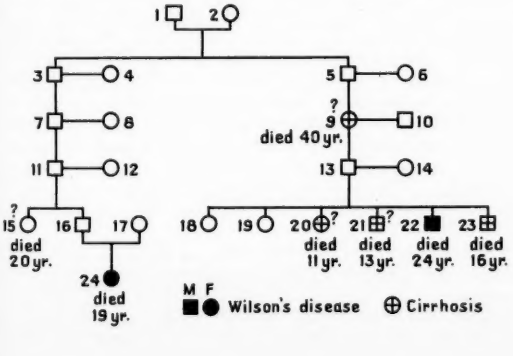
Report of a Family

The family tree is shown. Case 9 and two of six siblings (cases 20 and 21) are reported to have had jaundice and ascites for several months before death. All except the youngest of the six siblings had infective hepatitis in 1936. The two oldest sisters (cases 18 and 19), their parents, and the parents of case 24 are healthy: all have a normal serum-copper-oxidase activity, as estimated by Ravin's colorimetric test (1956).

Case 22 is described in the paper that follows this: the illness was acute, with liver cirrhosis but no neurological signs.

Case 23.—The patient was 14 years old when he was admitted to hospital on March 8, 1956. He had been healthy until six months previously, when he developed anorexia and malaise. He also complained of diffuse abdominal pain. His liver was enlarged and, after some months, his spleen also became palpable. He was jaundiced, at first intermittently, later continuously. He also developed ascites and had several hæmatemeses. Neurological signs, however, never appeared; no Kayser-Fleischer ring could be detected; and mentally he remained normal. He died on Oct. 3, 1957.

Investigations.—By transfusions after bleedings his hæmoglobin could be maintained around 85%, but his erythrocyte-sedimentation rate was often more than 100 mm. in an hour. His white-cell and red-cell counts were normal. Serum-bilirubin reached a maximum of 13 mg. per 100 ml. Thymol-turbidity was 0·10 (extinction). The prothrombin-proconvertin level was usually normal: on one occasion when it fell to 7% of normal, as measured by Owren's method (Owren 1951), it could be restored to 84% by injections of vitamin K. The serum-protein level fell from 7·2 to 5·2 g. per 100 ml. and the alkaline-phosphatase rose from 2·0 to 9·1 Bodansky units. The serum-iron was 42 μg., and the plasma-creatinine 1·2 mg. per 100 ml. There was inconstant proteinuria and no glycosuria. Repeated examinations showed abnormally high serum-copper-oxidase activity, a finding confirmed in November, 1956, by Prof. J. N. Cumings using a Warburg technique. The serum-copper at that time was 199 μg. per 100 ml., a high level often found in ordinary cirrhosis (Cumings et al. 1955).



Necropsy.—There was gross ascites; and the enlarged liver weighed 3200 g. Its surface was smooth but a tumour mass surrounded the vessels and bile-ducts at the hilum. Deposits were also found inside the liver and in the rectovesical pouch. Microscopic examination confirmed the diagnosis of severe portal cirrhosis and malignant hepatoma.

Case 24.—This intelligent schoolgirl had never been ill until June, 1953, when she noticed jaundice and nausea. She was admitted in September, 1953. The only abnormal laboratory finding was a prothrombin-proconvertin level of 36% of normal (Owren's method) and a moderately elevated thymol-turbidity (extinction 0·35). Her liver and spleen were not palpable, and she felt well enough to continue to go to school until March, 1955. During the next two months, however, she developed the characteristic signs of Parkinson's disease—the bent back, the adducted arms, the flexed elbows, and the shuffling gait. Her facial expression became fixed and her smile turned to a grin. She suffered from profuse salivation, severe dysarthria, and mild dysphagia; and, though she had no tremor, there was rigidity in all limbs. Her mind remained clear, and sensation and reflexes were normal; but she became emotionally unstable. During this time the signs of hepatic involvement also increased, and radiography revealed œsophageal varices. In May, 1955, she had a hæmatemesis and a year later she developed ascites. She was, however, not jaundiced, and further laboratory investigations showed only slight changes in her prothrombin-proconvertin level and thymol-turbidity.

Investigations and progress.—Her highest serum-bilirubin was 1·4 mg. per 100 ml.; her hæmoglobin oscillated around 85%; her erythrocyte-sedimentation rate was only slightly elevated; her serum-protein level was 6·3 g. per 100 ml.; her alkaline-phosphatase was 1·7 Bodansky units; her serum-iron was 136 μg., and her plasma-creatinine less than 1·0 mg., per 100 ml. There was an inconstant proteinuria and no glycosuria. Serum-copper-oxidase activity was much depressed on repeated examinations: in November, 1956, Professor Cumings found no activity, using the Warburg technique. The serum-copper was 48·3 μg. per 100 ml. In March, 1957, Kayser-Fleischer rings were seen on slit-lamp examination, and they later became visible to the naked eye.

She did not benefit from dimercaprol therapy; and, though anti-histamine drugs gave only symptomatic relief, she lapsed into coma after two hæmatemeses and died on April 6, 1957.

Necropsy.—The liver was about half the normal size and studded with yellow-brown nodules. On the cut surface these nodules were separated by broad bands of connective tissue which obliterated all normal structure. Microscopy showed fibrosis, regenerating and degenerating nodules, and infiltration by plasma-cells and granulocytes. The spleen was enlarged and firm. Several œsophageal varices were present. The cut surface of the brain and basal ganglia was normal, but microscopic examination showed degenerative changes in the nuclei lenticulares and in the cortex.

Discussion

In this family the diagnosis of hepatolenticular degeneration was confirmed biochemically and at necropsy in two cases (22 and 24). Three others had jaundice and ascites (9, 20, and 21), but they have not been examined by me. In case 23, however, repeated examinations during the course of the illness showed high copper-oxidase activity of the serum, a high serum-copper, and no neurological abnormality. The malignant hepatoma was probably secondary to the cirrhosis (Berk and Lieber 1941). These findings would ordinarily be regarded as ruling out the diagnosis of Wilson's disease.

When four of six siblings have died very young, all with symptoms and signs of liver damage, it is natural to suspect the same disease. How then can we explain

the different biochemical and necropsy findings in two brothers (cases 22 and 23)? Bearn (1957) showed that the serum-cœruloplasmin and the serum-copper rose to normal levels in three out of seven patients with Wilson's disease after treatment with œstrogens for periods up to 5 weeks. Enger (1958) described a case with normal serum-cœruloplasmin but with increased urinary excretion of copper in which Kayser-Fleischer rings were demonstrated and necropsy confirmed the diagnosis of hepatolenticular degeneration. These findings suggest that the biochemical lesions may be more variable than has been assumed. Œstrogens were not estimated in case 23 or in the case described by Enger. Hepatic damage, leading to impaired œstrogen breakdown and a normal serum-cœruloplasmin, cannot explain the high serum-copper-oxidase activity in case 23 at the onset of the illness. In case 22, moreover, a high urinary output of œstrogens was associated with very low serum-copper-oxidase activity.

Juvenile cirrhosis of the liver of unknown ætiology is very rare. Debré (1939) collected eighty-one cases from the literature and described a familial form. He cited Osler and Bramwell as thinking this as an abortive type of Wilson's disease.

From the family study here presented one must conclude either that the coexistence of Wilson's disease and juvenile cirrhosis in the same family was fortuitous or that the usual diagnostic criteria of hepatolenticular degeneration need to be revised.

Summary

In a family several members of which suffered from juvenile cirrhosis two members developed hepatolenticular degeneration. This was confirmed biochemically and at necropsy.

In the light of these findings the diagnostic criteria of hepatolenticular degeneration may have to be reviewed.

I wish to thank Prof. J. N. Cumings for his help with the copper estimations. My thanks are also due to Dr. P. Hanssen for his advice and permission to publish this paper.

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HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE)

A CASE DIAGNOSED BIOCHEMICALLY BEFORE CLINICAL MANIFESTATIONS

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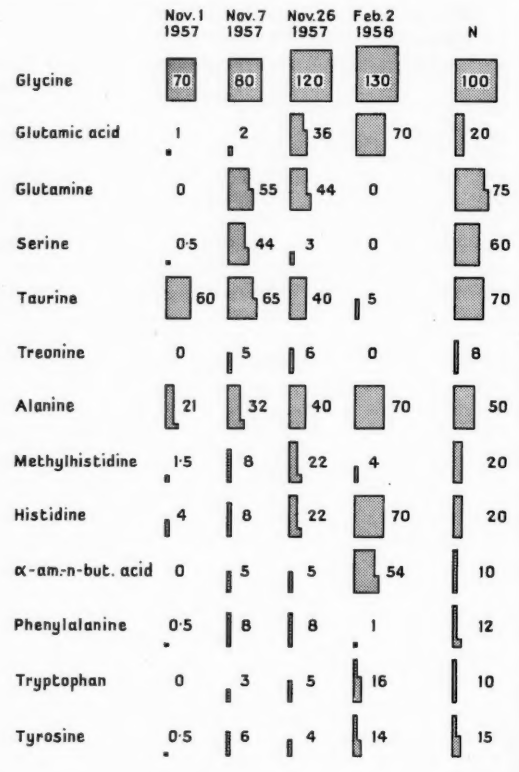
Ravin (1956) described a rapid diagnostic test for hepatolenticular degeneration, using the colorimetric estimation of serum-copper-oxidase activity. Holmberg and Laurell (1947) used *p*-phenylene-diamine as the substrate to measure serum-cœruloplasmin levels, and they found good correlation between serum-copper and serum-copper-oxidase activity. Scheinberg and Gitlin (1952), Bearn and Kunkel (1952), and Bearn (1953) confirmed these findings and recorded low serum-cœruloplasmin levels and diminished serum-copper-oxidase activity. Though this enzyme deficiency has been present in all cases so far reported (Bickel et al. 1957), it is not known whether it always precedes—and, if it does, by how long—the clinical manifestations.


Nov.1 1957
Nov.7 1957
Nov.26 1957
Feb.2 1958
N
Glycine 70 80 120 130 100
Glutamic acid 1 2 36 70 20
Glutamine 0 55 44 0 75
Serine 0·5 44 3 0 60
Taurine 60 65 40 5 70
Treonine 0 5 6 0 8
Alanine 21 32 40 70 50
Methylhistidine 1·5 8 22 4 20
Histidine 4 8 22 70 20
α-am.-n-but. acid 0 5 5 54 10
Phenylalanine 0·5 8 8 1 12
Tryptophan 0 3 5 16 10
Tyrosine 0·5 6 4 14 15

Using Ravin's colorimetric technique as a screening test, we found a patient who had a low serum-copper-oxidase activity but no symptoms or signs of hepatolenticular degeneration.

Case-report

He was 23 when he was first examined by us in August, 1956. He had had infectious hepatitis at the age of 3 but no symptoms or signs of liver disease or any other serious illness since then. There was a family history of hepatolenticular degeneration (see preceding paper).

Fourteen months later his liver and spleen were palpable but he was still feeling well. Potassium sulphide and a high-protein diet were prescribed. He continued to work as a fisherman until January, 1958, when he began to suffer from diffuse abdominal pain and distension. On Feb. 4, 1958, he was admitted to hospital. He had no neurological signs, no Kayser-Fleischer ring (examined with slit-lamp), and no mental symptoms. His blood-pressure was 130/80 mm. Hg. He had œdema of his legs and sacrum, and gross ascites. This made it impossible to feel his liver and spleen. He was jaundiced. The illness progressed rapidly: three weeks after his first symptom he became stuporous, and he died on Feb. 19.

Investigations.—In August, 1956, his serum-copper-oxidase activity was already very low, and it remained low on repeated estimations. In November, 1956, Prof. J. N. Cumings of London found no serum-copper-oxidase activity, using the Warburg technique, and a lowered serum-copper of 54·9 µg.

per 100 ml. A year later the prothrombin-proconvertin content of the plasma was 37% of the average normal, as estimated by Owren's method, but all other liver-function tests were normal. After he entered hospital in February, 1958, the laboratory tests showed: hæmoglobin 82% (Haldane); erythrocyte-sedimentation rate 9 mm. in an hour; red cells $3^1/_2$ million, white cells 6800, and platelets 174,000 per c.mm. Serum-bilirubin was 3·9 mg. per 100 ml., thymol-turbidity 0·25 (extinction), and the prothrombin-proconvertin content 11% of normal and resistant to vitamin K. The serum-protein level was 5·5 g. per 100 ml., and paper electrophoresis showed a great deficiency in the albumin and a considerable excess in the gamma-globulin fraction. The ascitic fluid had a protein content of 0·55 g. per litre and the same electrophoretic pattern. Plasma-creatinine was 1·0 mg. per 100 ml.; serum-alkaline-phosphatase 3·4 Bodansky units; serum-iron 116 μg. per 100 ml.; serum-uric-acid 7·7 mg., and blood-sugar 108 mg., per 100 ml. The urine contained no protein or sugar but an excess of urobilin. The 24-hour excretion of uric acid was 1·2 g. of œstradiol 9·6 μg., of œstrone 38·1 μg. (abnormally high), of œstriol 8·7 μg., and of copper 1852·5 μg. (abnormally high). Abnormal aminoacids were also demonstrated chromatograms, using the technique described by Dent (1948) (see figure).

Necropsy.—The liver was studded with yellow-brown nodules: it weighed 2050 g. Microscopy showed advanced nodular cirrhosis. The spleen was enlarged (625 g.) and had a smooth, firm pulp. The kidneys were normal. The diagnosis was portal cirrhosis due to hepatolenticular degeneration (Wilson's disease).

Discussion

The early clinical diagnosis of hepatolenticular degeneration can be difficult, since both the neurological and the hepatic symptoms vary greatly in severity and in their rate of progress. Cupruria and cœruloplasmin deficiency seem to be the commonest and earliest biochemical features: thus in Bickel's two youngest patients cupruria led to the diagnosis 2 years before the onset of symptoms and the low serum-copper levels suggested cœruloplasmin deficiency (Bickel et al. 1957). In our patient serum-copper-oxidase activity was greatly reduced more than a year before the first clinical signs appeared, and Cartwright et al. (1954) have shown that this corresponds to a similar decrease in cœruloplasmin-bound copper. Our findings thus support the view expressed by Bearn (1953) and others, that a deficient synthesis of cœruloplasmin may be the primary metabolic error.

Ravin's colorimetric method of serum-copper-oxidase estimation is a good screening test not only when symptoms or signs are already present, but also when investigating symptomless members of affected families.

Despite impaired liver function, abnormal aminoaciduria was absent in our patient 3 months before he died; it developed while he was under observation; and it diminished for glutamine, serine, taurine, and methylhistidine in the terminal stages of his illness. Similar findings were recorded by Bickel et al. (1957) and by Stein et al. (1954) who excluded renal tubular disease by plasma chromatography. In our patient the plasma-creatinine was normal; and we do not think that the terminal fall in the excretion of aminoacids could have been due to diminished glomerular filtration.

The pattern of the aminoaciduria seems to vary: our patient, for example, excreted an unusual amount of α-amino-*n*-butyric acid (see figure). We can suggest no explanation for this: nor do we know why the aminoaciduria developed so late.

As uric acid is often excreted in excess, leading to a diminished blood-uric-acid, Chalmers et al. (1957) suggested that this might be useful evidence in suspected Wilson's disease. In our patient, however, the blood-uric-acid was not reduced.

Summary

A case of acute hepatolenticular degeneration (Wilson's disease) is described in which the colorimetric estimation of serum-copper-oxidase activity led to the diagnosis more than a year before clinical manifestations.

Aminoaciduria developed late and the blood-uric-acid was not lowered.

We wish to thank Prof. J. N. Cumings, of London, and Dr. H. Palmer, of Drammen, for their help with the copper estimations, and Dr. P. Hanssen for his help and permission to publish this paper.

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AN END-TIDAL AIR SAMPLER FOR USE DURING ARTIFICIAL RESPIRATION

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ESTIMATIONS of carbon dioxide in samples of end-tidal air have been used extensively in normal subjects as a measure of the carbon-dioxide tension in arterial blood, and Rahn and Otis (1949) have devised a simple apparatus in which end-tidal air is collected in a small reservoir, from which samples may be withdrawn either continuously or intermittently. This apparatus has been widely used, but it is not suitable for patients receiving intermittent positive pressure respiration (I.P.P.R.). The need for a sampler of end-tidal air during I.P.P.R. is recognised (Inkster and Rees 1956, Linderholm 1956, Nunn and Pincock 1957), and this paper describes such a sampler * with examples of its use in conjunction with a flow-bridge carbon dioxide analyser.

* Messrs. H. G. East, 37, Oxford Road, Cowley, Oxford, propose to manufacture this sampler.

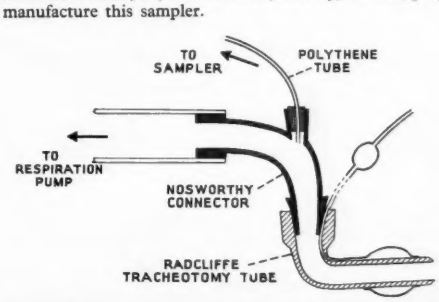


Fig. 1—Tracheotomy tube and connections. End-tidal samples are taken from the polyethylene tube.

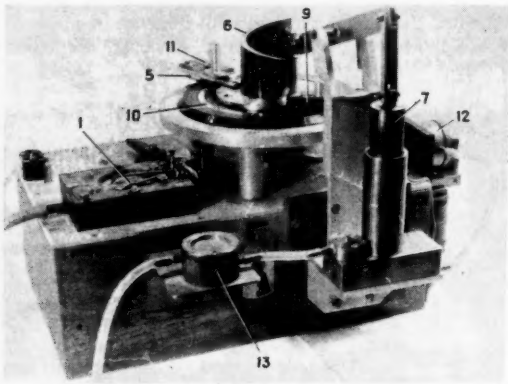


Fig. 2—End-tidal sampler. For description see text.

Description

At each respiration a sample is taken through a polyethylene tube (2 mm. bore) from close to the external end of the tracheotomy tube (fig. 1). The other end of the polyethylene tube is attached to the intake of the sampler. If the patient is in a tank respirator, satisfactory samples can be obtained by introducing the tube through the nose into the nasopharynx.

The principle of the sampler is that a piston is rapidly withdrawn in a cylinder at a selected interval after the onset of inspiration. The travel of the piston, and hence the size of the sample, varies inversely with the interval between the onset of inspiration and the taking of the sample; so the faster the respiratory rate the smaller is the sample taken from each breath.

The apparatus is illustrated in figs. 2 and 3.

The pressure-operated switch (1) is closed by the inspiratory rise in pressure in I.P.P.R., or the fall in pressure in the tank respirator, and this actuates a hold-on relay (2). This energises the solenoid (3) so that the clutch (4) is engaged and the travelling arm (5) and helical cam (6) begin to rotate. The piston (7) is therefore depressed in the sampling cylinder against a spring (8). As the travelling arm reaches the spring buffer (9), the brush on the travelling arm passes off the conductor rail (10) and breaks the hold-on relay circuit. The clutch is thus disengaged and the piston is pushed up by the spring (8), taking a sample and returning the travelling arm to the stop (11) at the resting position. The distance that the travelling arm moves before it reaches the buffer stop is easily adjustable, so that the sample can be taken at the appropriate part of the respiratory cycle. An electromagnetic valve (12) is closed during inspiration to prevent the positive pressure in the trachea causing air to pass into the sampler during inspiration. There is a non-return valve (13) immediately on the output side of the sampling cylinder.

The flow-bridge carbon-dioxide analyser (F.B.A.) used in these studies is that described by Cunningham et al. (1957).

The principle is that the gas to be analysed passes through a bridge system of capillary tubes, the carbon dioxide being absorbed on one side of the circuit with soda-lime (fig. 4). The pressure change across the bridge is directly proportional to the carbon-dioxide content of the gas being analysed.

Readings of the F.B.A. were converted to pCO_2 by means of a calibration curve determined on each occasion with carbon-dioxide-air mixtures, previously analysed in apparatus of the Haldane type. The capillary tubes constituting the bridge are kept in a water-bath at room temperature, and the apparatus has proved extremely stable in response and is free from drift over a period of many hours. Only small samples are required to feed this analyser, a total of about 60 ml. per min. being adequate.

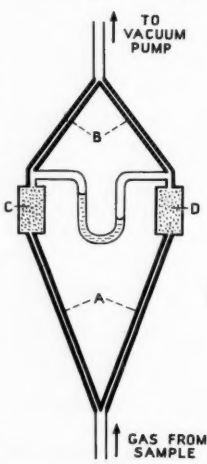


Fig. 4

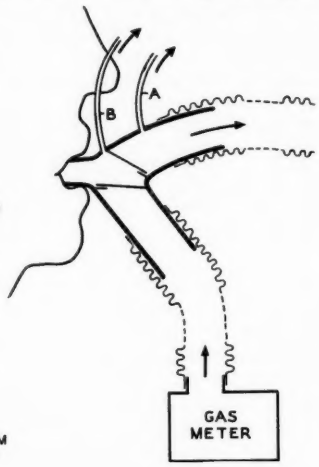


Fig. 5

Fig. 4—The principle of the flow-bridge carbon-dioxide analyser. A and B are capillary tubes. C contains soda-lime, D an inert substance.

Fig. 5—Respiratory valve. Samples were taken from A by the Rahn-Otis sampler and from B by the sampler here described.

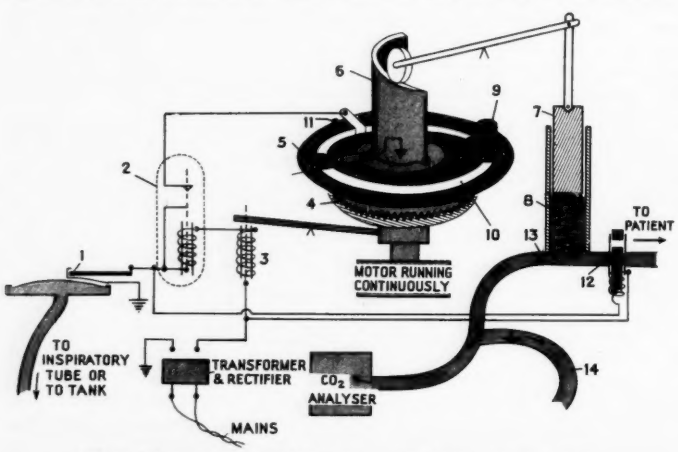


Fig. 3—Diagram of end-tidal sampler. For description see text.

The samples are stored in the tube (14, fig. 3).

This is 4 mm. in bore and 50 cm. long, and is open at one end, so that analysers requiring a continuous intake can be employed. The sampler has been designed to provide a slightly larger volume of air than is required to supply this analyser, and to confirm that the sample is sufficient the open end of the tube (14) may be dipped in water, when excess gas may be seen to escape.

The apparatus has been tested against the sampler described by Rahn and Otis (1949).

A normal subject breathed through a respiratory valve (Cunningham, Johnson and Lloyd 1956) in time with an I.P.P.R. pump, and voluntarily kept his tidal volume at a predetermined value by watching a gas-meter

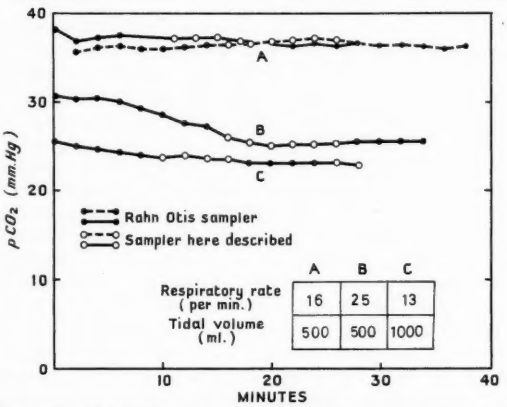


Fig 6—End-tidal pCO_2 in subjects breathing spontaneously. Samples were taken alternately with the Rahn-Otis sampler and the sampler here described.

connected to the inspiratory tube. Samples of end-tidal air were then taken either from the expiratory side of the valve by the Rahn-Otis sampler or from the mouthpiece by the sampler here described (fig. 5). End-tidal air from each sampler in turn was led to the analyser. With respiratory frequencies of 13-25 per min, and with tidal volumes of 500-1000 ml., no change was recorded in pCO_2 when one method of sampling replaced the other (fig. 6).

The end-tidal pCO_2 obtained with this sampler and analyser has also been compared with arterial pCO_2 on four occasions and on two patients. The results were:

Patient	Sample	End-expired pCO_2	Arterial pCO_2
A	1	22·9	27·35
	2	33·6	33·16
	3	32·6	30·82
B	1	21·5	24·44

The beginning of inspiration is a useful reference point in the respiratory cycle, and the sample can be taken at any interval after this point. Fig. 7 shows the effect of varying this interval at respiratory frequencies of 13–23 per minute. It is evidence that the timing of the sample is not critical, as the carbon-dioxide level maintains a plateau. Sampling at the extreme end of expiration is inadvisable because there is a danger of mixing the sample with inspiratory air.

The sampler has been used extensively on patients paralysed by poliomyelitis, polyneuritis, and myasthenia gravis, and on those with severe tetanus treated with curare. Fig. 8 illustrates the effect on the end-tidal pCO_2, in one patient, of varying the inspiratory pressure (fig. 8a), and the respiratory frequency independently (fig. 8b). Increasing the inspiratory pressure by only 33% reduces

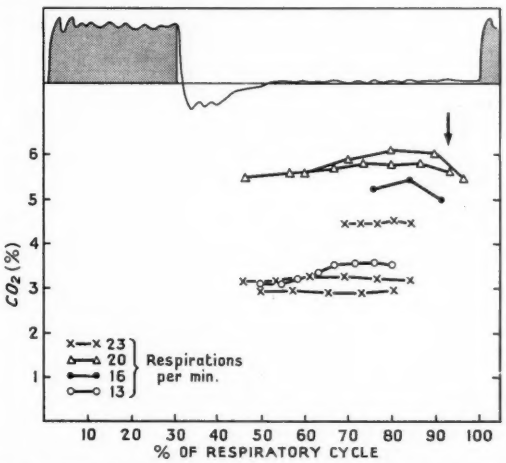


Fig. 7—The carbon-dioxide levels in the expired air when sampling is begun in varying parts of the cycle. At arrow the sample includes a small amount of inspired air. Upper record shows tracheal pressure, inspiratory period being hatched.

the pCO_2 slightly more than almost doubling the respiratory rate. This is partly because at higher respiratory rates the dead space is ventilated more frequently, and also because each inspiration is shorter and therefore of smaller volume (Spalding 1955).

Fig. 9 shows the end-tidal pCO_2 in two patients with respiratory weakness, each breathing alternately with artificial aid and by their own efforts. The carbon-dioxide levels in spontaneous breathing may be higher (fig. 9a) or lower (fig. 9b) than that during artificial respiration.

Fig. 9b is derived from a patient aged 54 with myasthenia gravis. On resuming artificial respiration after spontaneous breathing she would not tolerate a higher end-tidal pCO_2 than 28 mm. Hg, although she was comfortable, breathing spontaneously with end-tidal pCO_2 of about 36 mm. Hg.

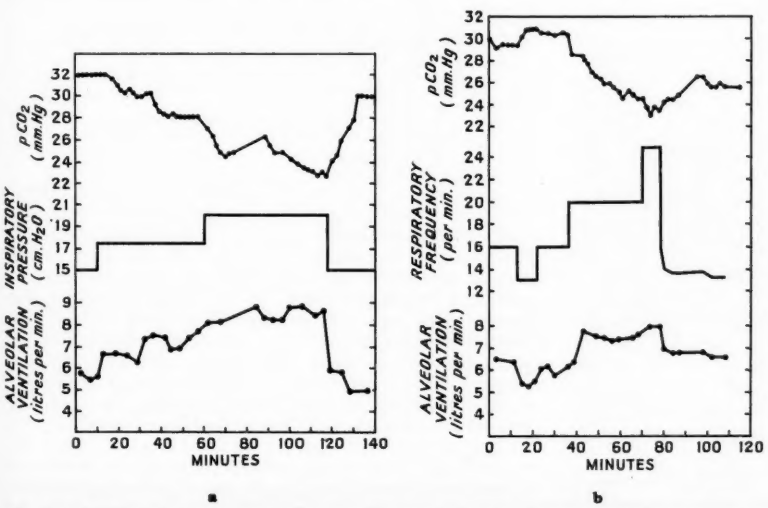
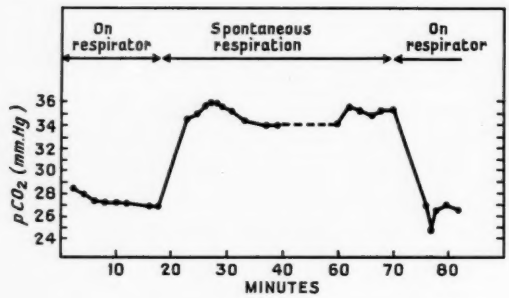


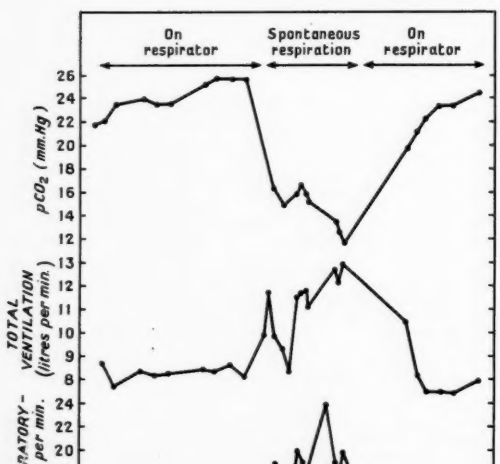
Fig. 8—(a) Effect of altering inspiratory pressure, respiratory frequency remaining at 16 per min. (b) Effect in same patient as in (a) of altering respiratory frequency, inspiratory pressure remaining at 15 cm. water. In calculating alveolar ventilation a constant dead space of 100 ml. has been assumed.

Discussion

The clinical observation which we regard as indispensable in the assessment of a patient's ventilation is the measurement of the respiratory minute volume, allow-



a



b

Fig. 9—Paretic patients breathing alternately without assistance and with a respiration pump. In (a) the patient selected a higher and in (b) a lower pCO_2 when breathing spontaneously.

ances being made for the dead space. It is sometimes desirable, however, to use an additional method. The value of estimation of end-tidal air pCO_2 as a measure of arterial pCO_2 has been demonstrated both in subjects breathing spontaneously (Suskind et al. 1950, Galdston et al. 1951, Saxton 1953), and in patients receiving artificial respiration by I.P.P.R. (Linderholm 1956, Walley 1957) or in tank respirators (Collier et al. 1954). The pCO_2 in end-tidal air can, moreover, easily be measured with considerable precision, whereas the estimation of pCO_2 in blood is much more liable to inaccuracies (Dejours 1956, Shepard and Meier 1957). Walley (1957) and Linderholm (1956), however, have shown that in patients whose lungs are abnormal this relationship does not necessarily hold.

The sampler here described takes only 10 ml. of end-tidal air per breath at 13 respirations a minute, and this ensures that concurrent measurements of the respiratory minute volume are not disturbed. As the respiratory rate rises, the size of each sample decreases. It follows that samples taken from children are appropriately smaller than that for adults, and yet the amount of sample per minute remains approximately constant. The constancy of its output has enabled us to use a continuous-flow analyser which is simple, accurate, and, unlike many analysers, linear in response. The sampler is also convenient when using single-sample analysers, such as the Haldane apparatus or Drager analyser, which are remarkable respectively for accuracy and convenience.

We have found this apparatus useful as a check when there is any doubt about the level of ventilation, especially in children. It is also instructive to follow the effect of changes in ventilation on the end-tidal pCO_2 (figs. 8 and 9). Fig. 9 demonstrates that a patient on artificial respiration may demand a lower pCO_2 than normal—a phenomenon also observed with tank respirators. It also shows that, after long-continued artificial respiration, the patient's respiratory centre is not necessarily reset to a new pCO_2 and that when he is allowed to breathe spontaneously the pCO_2 he maintains may be above or below that to which he has become accustomed on artificial respiration. In these circumstances it is apparent that pCO_2 is not the only factor in the patient's control of his own respiration, and since in both subjects the end-tidal pCO_2 is below normal this factor is unlikely to be oxygen lack.

Summary

Apparatus is described which repeatedly samples end-tidal air in patients receiving artificial respiration either by intermittent positive pressure or in a tank respirator. The more rapid the respiratory rate the smaller the sample, so the volume of sample per minute is roughly constant.

This apparatus has been used with a bridge-type continuous-flow carbon-dioxide analyser. Examples are given of the effect on end-tidal pCO_2 of changes in respiratory rate and of tidal air. In paretic patients who are able to breathe spontaneously for short periods, end-tidal pCO_2 during spontaneous respiration may be higher or lower than that on artificial respiration.

Dr. D. J. C. Cunningham and Dr. B. B. Lloyd of the department of physiology, Oxford University, have given much valuable advice, for which we are grateful.

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"Soon the technologists will become very numerous, and they will reach positions of great power in industry and in the government of the nation. They will replace many of the lawyers and accountants, the bankers and financiers, the executives and administrators trained in the humanities, the non-scientists who today have power and responsibility for leadership. When that stage is reached, as it shortly will be, where will the new leaders lead, and how will they influence society? History cannot tell us, for science and technology have never been in this position before, but it is plain common sense that the ideals a man cherishes and the wisdom he brings to their pursuit derive largely from his education. Where the scientist and the technologist will take our children depends on how we are educating the scientist and the technologist today. It depends too on how we are choosing those whom we educate."—ROBERT AITKEN, report of the vice-chancellor and principal, University of Birmingham, 1958.

RETROGRADE AORTOGRAPHY IN ACUTE DISSECTING ANEURYSM OF THE AORTA

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SUCCESSFUL surgical management of dissecting aneurysm of the aorta has now been reported in 13 cases (DeBakey 1955, 1956, Warren et al. 1956, Swann and Bradsher 1956, Martin and Muir 1958). In 4 of these the dissection was acute and in the others subacute or chronic. Nevertheless the condition remains a serious one and the mortality, immediate and remote, of treated and untreated cases is high. Pyke (1956) has shown that the diagnosis can often be made on the history and clinical findings alone, assisted on occasion by radiography of the chest. Eastcott and Sutton (1958) recorded the demonstration of the double aortic channel by aortography in a chronic case. Little use of contrast media appears to have been made in acute cases, and indeed they are seldom indicated. They may, however, be of value in diagnosis in the doubtful case, since the presence and extent of the dissection and the degree of obstruction of the aorta and its branches can be shown. Halliday (1952) reported a case demonstrated by angiocardiography in the acute stage; and Warren et al. (1956) described another acute dissection confirmed by aortic catheterisation.

Aortography may be of greater value when dissection involves the iliac arteries with obstruction of their lumen, and may help to determine correct surgical treatment. Aortography by percutaneous retrograde femoral catheterisation results in slight inconvenience or risk even to a seriously ill patient. A case of acute aortic dissection with obstruction of the right iliac artery is reported here to illustrate the method and to show how surgical management might have been modified, perhaps with a successful outcome, had the full significance of the radiographic findings been appreciated at the time.

Case-report

A man of 53, a crane driver, who had been treated for chronic myeloid leukæmia for one year, had sudden severe pain in the chest while at work on Nov. 29, 1957. The pain radiated to the back, abdomen, and right leg, which during the next fifteen minutes became cold, numb, and powerless. He managed to walk 20 yards and drove his car 2 miles before being brought to hospital by ambulance and was admitted under the care of Dr. S. R. F. Whittaker. He was only mildly shocked, though in considerable pain. He had a collapsing pulse of 84 (blood-pressure 130/60 mm. Hg in right arm, 140/70 in left arm). Systolic and diastolic murmurs were heard over the base of the heart and these were conducted down to both groins. No murmurs had been present a year previously. The right leg was cold and white below the knee, with absence of all pulses, loss of power, and anæsthesia. There was tenderness over the right femoral and iliac arteries. An E.C.G. gave no evidence of coronary thrombosis. A chest X-ray showed some widening of the mediastinal shadow. Examination of the urine disclosed no abnormality.

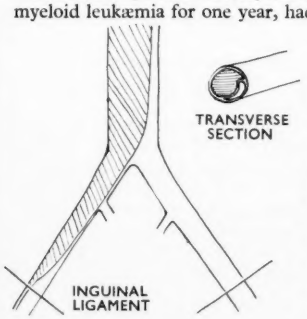

Fig. 1—Dissecting aneurysm extending into and occluding the right iliac artery.

A diagnosis of dissecting aortic aneurysm was made, although the absence of severe shock and the unilateral femoral-artery obstruction suggested an embolus. Exploration of the right iliac vessels was undertaken several hours later and confirmed the presence of a dissecting aneurysm. Fig. 1 shows diagrammatically the distribution of the dissection of the aneurysm. A fenestration type of procedure (fig. 2), with division and resuture of the external iliac artery, produced no appreciable improvement in the circulation of the leg. His general condition next day was otherwise satisfactory but hæmaturia developed for the first time, suggesting serious renal-artery involvement. A more proximal decompression of the aneurysm seemed necessary to prevent progressive renal damage and restore the circulation of the right leg, and this was carried out on Dec. 1, immediately after a retrograde femoral aortogram (fig. 3). The catheter can be seen passing up into the aorta and the contrast medium outlines the obstruction. The renal vessels are not filled and the left iliac artery is faintly shown, but there is no shadow on the right side. Fig. 4 shows the operation performed in view of the distal fenestra created at the previous operation. An aortic bifurcation homograft was inserted between the divided aorta, the right femoral artery and the left common iliac artery. A window was made in the inner coat of the aorta below the renal vessels. Satisfactory circulation was restored to the lower limbs and the operation was well tolerated. Oliguria persisted, however, and

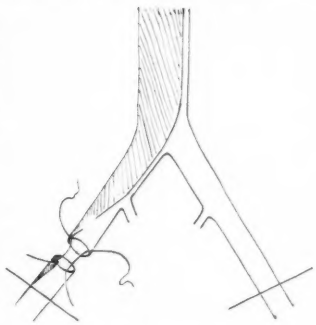

Fig. 2—First operation.

Fig. 3—Retrograde aortogram showing almost complete obstruction of the aorta above the renal arteries. The left common iliac artery is poorly outlined. No contrast medium is visible in the right common iliac artery.

despite the adoption of a modified Bull's regime, the blood-urea rose to 270 mg. per 100 ml., and the patient died five days after the second operation.

Necropsy showed that the site of origin of the aneurysm was a tear in the aortic wall, 3 cm. in length, and 2 cm. above the aortic valve. The wall of the right renal artery was dissected, and the left renal artery was compressed by surrounding intramural aortic clot but there was no dissection of its wall. There was a small re-entrant rupture of the aneurysm 2 mm. in length, back into the lumen of the aorta just above the orifice of the right renal artery. Clot was present only in the lower part of the dissection. Both kidneys were swollen and pale, and histological section showed changes resulting from acute ischæmia. The spleen and liver were enlarged by myeloid infiltration. The anastomoses were intact. Sections of the aortic wall showed cystic medial necrosis.

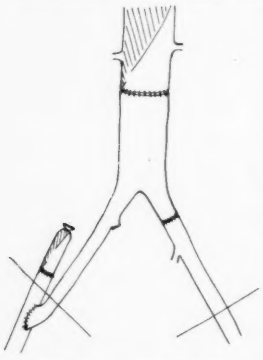

Fig. 4—Second operation.

Discussion

The death of this patient from uræmia strongly suggests that the operations failed to relieve the obstruction to the renal arteries, although delay between the two operations may have produced irreversible renal damage. It is felt in retrospect that the demonstration by aortography of bilateral renal-artery obstruction should have made obligatory a decompression fenestration procedure on the aneurysm in the thoracic aorta, and that this should have been supplemented by a further decompression of the right iliac artery. DeBakey, whose experience of the surgical treatment of these aneurysms is unrivalled, has certainly emphasised the value of this proximal decompression above the renal arteries. When no obstruction of the renal or other main abdominal vessels has resulted from the aneurysm, however, the fenestration decompression procedure may be successful in the abdominal aorta at a lower level. Martin and Muir (1958) in fact have reported success after such an operation carried out in the iliac artery obstructed by the extension into it of an aortic dissection. A similar operation by Gurin et al. (1935) was unsuccessful. In the patient described here the procedure failed to relieve the obstruction of the iliac artery, perhaps because it was carried out at too low a level. Even if relief had followed, it is still doubtful whether decompression of the renal arteries would have been sufficient. The importance of detecting obstruction of the renal arteries should therefore be emphasised, and it seems that retrograde aortography can be an effective help in deciding what to do.

Summary

Surgical treatment of a dissecting aneurysm of the aorta with obstruction of the right iliac artery was unsuccessful. Retrograde aortography can help in the management of such cases.

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ACUTE HEPATIC NECROSIS FOLLOWING IPRONIAZID THERAPY

VALUE OF GLUTAMIC-OXALOACETIC TRANSAMINASE ESTIMATION IN EARLY DETECTION

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ACUTE hepatic necrosis occasionally follows administration of iproniazid. This complication is rare, occurring in 1 in about 2000 treated patients; but it is known to have a bad prognosis with a mortality of about 15% (*New England Journal of Medicine* 1958).

We report briefly the clinical findings in 2 patients in whom acute hepatic necrosis developed after iproniazid therapy. One of these patients, who recovered, was being treated for intractable angina of effort. The other, who died, was taking part in a trial of this drug in the treatment of depression (Pare and Sandler 1959).

When, during this trial, it became known that liver damage occasionally follows drug treatment, we considered it advisable to carry out tests of liver function in order to detect, if possible, any early changes which might herald this complication. Besides "standard" tests of liver function, which showed no significant abnormality in the patients tested routinely (Pare and Sandler 1959), serum glutamic-oxaloacetic transaminase (G.O.T.) levels were obtained. Serum G.O.T. estimation has recently come into extensive use as an index of hepatocellular damage (Pryse-Davies and Wilkinson 1958). We will present evidence that significant changes occurred in some of the patients in the trial.

Case-reports

Case 1.—A 38-year-old male compositor had angina of effort which had begun six months before a posterior myocardial infarction on June 4, 1957. After this acute illness his angina became more severe, and on March 18, 1958, treatment with iproniazid 50 mg. b.d. was started. His exercise tolerance improved dramatically, and, despite side-effects such as constipation, disturbance of sleep rhythm, and impotence, the patient was pleased with life.

On May 27, 1958, he reported that he had been passing dark urine for several days. He was icteric and had a serum-bilirubin level of 8 mg. per 100 ml., an alkaline-phosphatase level of 18 King-Armstrong units per 100 ml., but normal flocculations. Iproniazid was stopped. A week later his serum-bilirubin had increased to 20 mg. per 100 ml. and flocculations were now strongly positive. He was admitted to hospital and treated with neomycin and low-fat, low-protein diet.

Apart from slight drowsiness in the first two days in hospital, there was no impairment of consciousness. After two weeks he became clinically less jaundiced and had become well enough to be discharged from hospital by June 28, 1958. When seen as an outpatient on July 15 he was feeling fit. Serum-bilirubin was 1·3 mg. per 100 ml., and serum G.O.T. had fallen from very high levels to 43 units per ml. A fortnight later, the serum G.O.T. had dropped to within normal limits.

Case 2.—A 56-year-old housewife, with myxœdema controlled by thyroid tablets, presented with recurrent depression. She responded to iproniazid after electroconvulsive therapy had failed to result in improvement. Iproniazid had been started on Feb. 3, 1958, in dosage of 400 mg. daily, reduced

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to 300 mg. daily within three days, to 200 mg. daily on April 14, and, after discharge from hospital, to 100 mg. daily on May 12. Placebo was substituted during the period March 13–26 with relapse of her depression.

Iproniazid was stopped on June 9 because of "dizzy" attacks which had resulted in the patient falling and bruising her face. Within a week she again became depressed and agitated and on June 19, ten days after iproniazid had been discontinued, she became jaundiced and was admitted to hospital. She was found to have mild hepatitis with serum-bilirubin 3·7 mg. per 100 ml., thymol turbidity 8 units, and alkaline phosphatase 22 K.A. units per 100 ml. On July 5 she became delirious, lapsing into coma during the next two days. Her jaundice rapidly deepened, and she died on July 12.

The main findings on postmortem examination, which was performed on the same day by Dr. J. L. Hamilton-Paterson, were a small shrivelled liver which macroscopically and microscopically was typical of acute hepatic necrosis. The almost complete absence of thyroid tissue confirmed the presence of myxœdema.

Dr. A. N. Davison kindly examined a portion of liver tissue by manometric methods, and could find no monoamine-oxidase activity whatever.

Methods and Materials

Serum G.O.T. activity was estimated by the colorimetric method of Reitman and Frankel (1957). Serum from 29 patients taking part in a trial of iproniazid (Pare and Sandler 1959) was assayed before (18 patients) and at intervals during treatment with the drug. Doses of 150–450 mg. a day for two to forty weeks were used.

Results

The results are shown in fig. 1.

Values were within normal limits of 8–28 units per ml. at 20°C in all sera obtained before drug treatment. In 9 patients levels above the normal range were found during iproniazid administration.

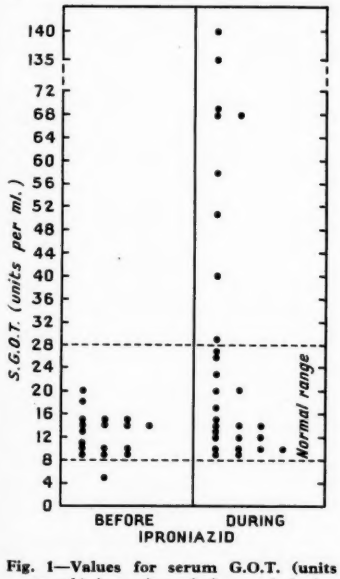

Fig. 1—Values for serum G.O.T. (units per ml.) in patients before and during treatment with iproniazid.

Values of 40 units or above were considered as indications for stopping treatment. Levels then gradually dropped, taking about four to six weeks to return to normal. A typical finding is shown in fig. 2. There did not appear to be any correlation between, on the one hand, dosage or the length of time that the patient had been taking the drug and, on the other hand, rise in G.O.T.

Discussion

Although it cannot be stated categorically that the illness in the 2 cases discussed here was directly due to iproniazid, acute hepatic necrosis following therapy with this drug has now been described sufficiently often to make the association highly likely (Bosworth et al. 1955, Benaim and Dixon 1958, Frantz 1958, Smarr et al. 1958, de Verteuil and Lehmann 1958, Zetzel and Kaplan 1958). Certainly there did not appear to be any other predisposing cause.

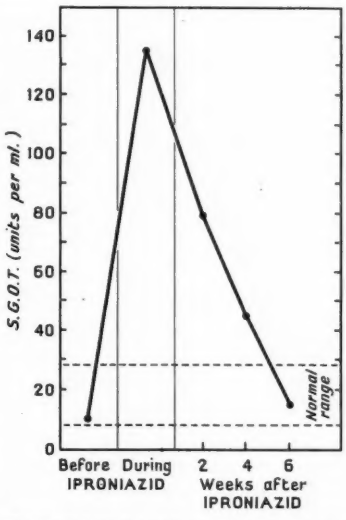

Fig. 2—Values for serum G.O.T. (units per ml.) in a patient before, during, and after treatment with iproniazid.

Serum G.O.T. levels were found to be raised in almost a third of the patients examined. In the absence of liver-biopsy specimens we have no direct evidence that this abnormal finding was a consequence of hepatic damage. Indeed, it is known that a rise in serum G.O.T., which is a sensitive index of cell injury, may occur in various clinical conditions. However, raised levels such as we observed would probably have given rise to clinical signs had they stemmed, for example, from myocardial infarction (Baron et al. 1958). That the "standard" tests of liver function showed no abnormality is not incompatible with our interpretation; for, with the possible exception of serum-alkaline-phosphatase, these tests do not measure liver-cell damage. Further, patients with a degree of hepatic necrosis sufficient to give rise to unequivocally abnormal "standard" tests characteristically show serum G.O.T. levels considerably greater than those observed in our series.

A further possibility deserves to be considered. We do not at present know the effect of monoamine-oxidase inhibitors, as a group, on serum G.O.T. levels. Possibly the finding is common to the class as a whole and is unrelated to actual cell damage. Until other similar drugs become available for clinical trial, however, this cannot be checked.

Although we have no direct evidence that the rise in serum G.O.T. in our patients was a consequence of liver damage, nevertheless, because of the known occurrence of acute hepatic necrosis in a small proportion of patients on treatment, we believe that it would be safer to assume the direct association until further evidence accrues. We are proposing to undertake further studies, experimental and clinical, in an attempt to elucidate this problem. If our hypothesis is correct, then the earliest detection of hepatocellular damage by means of serial serum-G.O.T. estimations may be of great importance. Experimental observations (Chessin et al. 1957), our own findings of a delayed return of a raised G.O.T. to normal levels after stopping iproniazid, and the occurrence of jaundice up to three weeks after withdrawing the drug (case 2) (Smarr et al. 1958), all indicate that the action of iproniazid is long-continued.

Now that the colorimetric assay of serum-G.O.T. activity is becoming routine in so many clinical laboratories

(Baron et al. 1959) its use in patients undergoing treatment with iproniazid may help to rob such a potentially valuable drug of its main hazard to life. We would suggest that any rise detected in routine weekly serum-G.O.T. estimations should, in the present state of our knowledge, be treated as presumptive evidence of early liver damage, and discontinuance of the drug seriously considered. In the interests of the patients' safety we feel that the test should form as routine a part of the therapeutic regimen with iproniazid as is assay of prothrombin activity in anticoagulant therapy.

Summary

2 cases of acute hepatic necrosis following iproniazid administration are described.

Estimation of serum-glutamic-oxaloacetic transaminase (G.O.T.) in 29 patients undergoing treatment with iproniazid showed raised levels in 9. The significance of this finding is at present uncertain.

In the interests of the patients' safety a raised serum G.O.T. level should be regarded as presumptive evidence of early hepatic damage, and discontinuance of the drug should be seriously considered.

We should like to thank Dr. F. P. Lee Lander, Dr. Denis Leigh, and Dr. L. I. M. Castleden for permission to publish details of patients under their care; Dr. D. N. Baron for constructive criticism; Dr. J. Marks, of Roche Products Ltd., for helpful advice; and Miss M. G. Barthen and the staff of the department of chemical pathology, Royal Free Hospital, for technical assistance.

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THE DANGERS OF INDWELLING POLYETHYLENE CANNULÆ IN DEEP VEINS

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THIS paper reports some experiences with indwelling polyethylene cannulæ in deep veins during the treatment of severely burned patients. The cannulæ were used not simply for infusing fluids, which can be done equally well through superficial veins, but for withdrawing numerous samples of blood for hæmatocrit, blood-volume, and electrolyte estimations. They also allow infusion of 50% dextrose in anuric patients, avoiding the frequent changes of infusion site necessitated by thrombophlebitis.

In the management of anuria many workers have used polyethylene cannulæ in deep veins (Chalmers and Fawns 1955, Chambers and Smith 1957, *Lancet* 1957, Russell et al. 1954). Taylor (1957), however, regarded the method as hazardous because of venous thrombosis around the cannula. Verel (1958) recommended that it should be used for blood-transfusions where these were expected to last more than 24 hours; but Moncrief (1958), from his experience at the Brooke Army Hospital, thought this method of transfusion should be reserved for cases in which other methods had been exhausted.

Materials and Method

Between January, 1956, and June, 1958, 166 cases of burns requiring colloid infusion were admitted to the Birmingham burns unit. In fifteen of them a polyethylene cannula was passed into a deep vein.

The cannula (1 mm. or 1·5 mm. in diameter) was filled with water and placed in a cylindrical glass tube to keep it straight. The glass tube was filled with water and the whole boiled for 15 minutes, after which it was cooled quickly so that the physical properties of the polyethylene should be changed as little as possible. The changes noted included some shortening and a noticeable increase in bore.

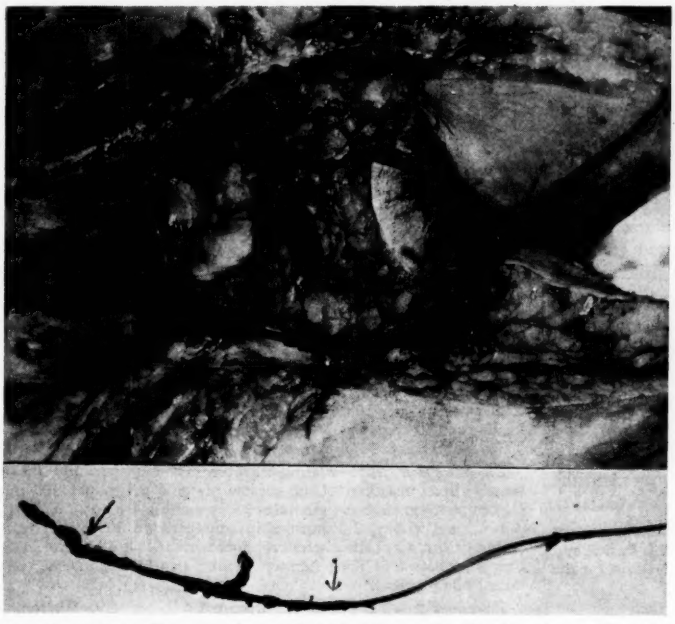
The cannula was introduced through an incision into a superficial vein and passed into the inferior vena cava (11 cases) or the subclavian vein (4 cases). In one patient with a 95% burn (case 5) the incision had to be made through burned skin. Blind intubation of the deep veins was not used.

Results

Details of the cases are shown in the table.

PATIENTS WITH INDWELLING CANNULÆ

Case no.	Age	% of body surface burned	Duration and site of cannula	Outcome
1	6	55	1/2 day (10 hours). Common iliac vein. Became blocked	No clinical signs or symptoms of venous occlusion
2	8	50	11 days (264 hours). Subclavian vein	,,
3	7	43	12 days (240 hours). Subclavian vein	,,
4	17	40	14 days (336 hours). Subclavian vein. Clot occluded the tip	,,
5	42	95	1 1/2 days (34 hours). Iliac veins and inferior vena cava	Antemortem thrombosis at tip of cannula and along vein
6	5	90	5 days (120 hours). Iliac veins and inferior vena cava	Renal failure. Antemortem thrombosis
7	20	65	5 days (120 hours). Axillary vein. Became blocked	Postoperative acute dilatation of stomach (18th day). Septic thrombus, with pyæmia. Septic infarction of lungs
8	11	65	1 1/2 days (34 hours). Iliac veins and inferior vena cava	Renal failure. Small antemortem thrombus at tip of cannula
9	5	65	5 days (126 hours). Iliac veins and inferior vena cava. Became blocked	Renal failure. Antemortem thrombosis
10	2	65	2 days (48 hours). Iliac veins and inferior vena cava	Antemortem thrombosis of common iliac and femoral veins
11	24	60	Left: pulled out by patient after 4 1/2 days (108 hours). Right: another inserted (48 hours)	Left: adherent antemortem thrombus. Right: recent friable antemortem thrombus
12	62	40	5 days (126 hours). Iliac veins and inferior vena cava	Pneumonia. Antemortem thrombosis
13	67	40	1 day (21 hours). External iliac vein	Renal failure. ? septicæmia. No thrombosis
14	60	30	2 days (48 hours). Iliac veins and inferior vena cava	Pulmonary embolism from deep-vein thrombosis in leg. Small platelet thrombus at site of cannula
15	5	23	1 day (24 hours). Iliac veins and inferior vena cava	? air embolism



Case 11—An indwelling cannula was first introduced into left iliac veins. When this was pulled out by patient on 5th day, another was introduced on right side. The photograph shows the condition at necropsy. Above: catheter in right external iliac vein surrounded by recent antemortem thrombus. (On left side is an older adherent thrombus.) Below: catheter with adherent clot after removal.

Survivors.—Four of the fifteen patients survived (cases 1–4). Their cannulæ were in the deep vein for a mean period of $8^1/_2$ days (212 hours): in three of the four patients they were there for more than 4 days. In none of these cases was there any evidence of deep-vein thrombosis.

Fatal cases.—In the eleven fatal cases necropsy was performed (cases 5–15). All except one (case 13) showed antemortem thrombosis. The cannulæ had been in the vein for a mean period of 3 days (70 hours). In the cases whose cannulæ had been in place for less than 48 hours the thrombosis was not extensive. In those whose cannula had been in place for more than 4 days thrombosis was extensive and the vein was partly (though never completely) occluded by the thrombus, which was usually fixed firmly to the vein wall.

Three cases require further comment:

CASE 7.—At necropsy the thrombus in the axillary vein extended along the cannula to the superficial vein and was obviously infected. There were septic infarcts of the lung with early abscess formation.

CASE 14.—This patient died of pulmonary embolism, but necropsy showed that the thrombus originated in a deep vein in the leg—not from the cannulated inferior vena cava.

CASE 15.—This child died unexpectedly, with signs of congestive cardiac failure, on the 12th day after burning. At necropsy air-bubbles were noted in the cerebral vessels. Although there is no conclusive proof that she died of air embolism, air may have entered the transfusion set through a faulty connection.

Site of thrombosis.—The thrombus most often formed at the tip of the cannula, extending distally. Another site was where the cannula entered the superficial vein, injuring the endothelium. From this point it extended proximally. In case 11 the thrombus had surrounded the cannula along its entire length, and when the cannula was withdrawn at necropsy a cannulated thrombus was left (see figure).

Functional efficiency—As regards management, the cannulæ were convenient and worked well. As a rule they made it easy to withdraw blood samples without discomfort to the patients, and to inject irritant fluids without thrombosing superficial veins. At times, however, the infusion fluid flowed into the vein but no blood could be withdrawn: this was afterwards shown to be due to a ball-valve type of thrombus. Usually, in time, the cannula became completely blocked.

Discussion

Incidence of thrombosis.—Our cases suggest that in severely burned patients silent thrombosis often develops round cannulæ kept in the deep veins (10 out of 15 cases). The fact that the common sites of thrombosis were where the cannula pierced the vein wall or where the tip rubbed against it suggests that thrombosis is started by damage to the endothelium.

Hazards of thrombosis.—There were no deaths from pulmonary embolism (if case 14 is excluded) nor was embolism ever suspected clinically. This was also the experience of Moncrief (1958). Perhaps traumatic thrombosis does not produce emboli so easily as thrombosis resulting from stasis.

The most serious complication was a septic thrombosis (case 7). The thrombus extended from the superficial veins along the cannula to the axillary vein, and there were septic infarcts and multiple abscesses in the lungs.

The risk of air embolism—always present in intravenous cannulation—is increased when the cannula is passed into the great veins, where a negative pressure may actively suck fluid (and air) into the circulation. This risk can be reduced by having as few junctions as possible in the apparatus and ensuring that they are secure and airtight.

Prophylactic measures.—Anticoagulants were not used. In some of these patients excision of burned tissue was carried out as a primary measure, and anticoagulant therapy was therefore contraindicated. Moncrief (1958) expected little benefit from the use of anticoagulants locally, and recommended systemic therapy. It is still debatable whether anticoagulant therapy would be beneficial.

Sepsis is probably more preventable.

Reasonable precautions include: proper sterilisation of the cannula by boiling for 15 minutes; meticulous technique in its introduction; careful closure of the skin incision; and antibiotic cover appropriate to the flora of the cannula incision if this becomes infected. Because withdrawal of blood involves disconnecting and handling the cannula, the risk of infection may be increased by frequent sampling. It is lessened if one person is responsible for handling the infusion and withdrawing specimens.

Indications.—In spite of the risks, indwelling venous cannulæ are sometimes very valuable. They are indicated:

1. When blood samples are required frequently and are not readily obtainable from superficial veins.
2. For infusion of irritant fluids such as 50% glucose.
3. On the rare occasions when intravenous fluids are necessary yet cannot be given through superficial veins.

Summary

Polyethylene cannulæ in deep veins were used in 15 extensively burned patients. They facilitated frequent blood sampling and the infusion of nutritive fluids.

In ten of the eleven fatal cases antemortem thrombosis was found at necropsy. In the remaining fatal case, and in the four patients who survived, there were no signs of thrombosis.

One patient developed a septic thrombus: this was not the immediate cause of her death. Another possibly died from air embolism.

Limited indications for the use of indwelling cannulæ in deep veins are suggested.

I wish to thank Mr. D. M. Jackson for his help and encouragement in the preparation of this paper. I must also thank Dr. J. P. Bull and Mr. J. S. Cason for their helpful criticisms, and Dr. S. Sevitt for the necropsy findings.

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A CASE OF XANTHOMATOUS BILIARY CIRRHOSIS TREATED WITH ETHYL LINOLEATE

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OBSERVATIONS in this laboratory (Kinsell et al. 1952, 1955, 1958) that diets rich in polyunsaturated fatty acids lower the plasma total-lipid, cholesterol, and phospholipid levels suggested the trial of large doses of ethyl linoleate in the treatment of a patient with primary biliary cirrhosis whose plasma showed the characteristic gross elevation of these lipids.

Case-report

A white woman, aged 42, complained of the insidious onset, early in 1956, of tiredness, generalised pruritus, occasional upper abdominal discomfort, and mild jaundice with dark urine and intermittently pale stools. Investigation elsewhere showed that the jaundice was of an obstructive type. Exploration of the extrahepatic biliary tract showed no abnormality but cholecystectomy was performed. Unfortunately a liver biopsy was not taken. Convalescence was uneventful but her symptoms persisted. In March, 1957, she first noticed small non-tender yellow deposits in the creases of the fingers and the palms. Within a few months similar lesions involved the skin of all parts of her body.

On admission to the institute on Feb. 10, 1958, she complained chiefly of severe tiredness, weakness, generalised pruritus, and difficulty in flexing the fingers. She had lost about 20 lb. in weight since the onset of her symptoms.

She had undergone an appendicectomy, two cæsarean sections, and an operation for lumbar-disc protrusion; but from 1951 until 1956 she had not been ill and had received no drugs. She had never been jaundiced before and had not been in contact with toxic chemicals.

Physical Examination

Weight 117 lb. General nutrition good. Scleræ jaundiced. Skin light olive colour, dry and scratched. Numerous xanthomata, 1–10 mm. in diameter, were seen on the hands, feet, face, and ears, and over the knees and elbows. Some deposits were felt in the Achilles tendons and a few were seen in the buccal mucosa. The liver edge was firm and regular and was felt 2 cm. below the costal margin. The spleen was not felt and no spider angiomata were seen.

Laboratory Findings on Admission

Plasma-lipids.—Total lipids 3900 mg. per 100 ml. Cholesterol: total 1490 mg. per 100 ml., free 1340, ester 150. Phospholipids (as lecithin) 2840 mg. per 100 ml. Dihydroxycholate 36 μg per ml. Trihydroxycholate 34 μg per ml.

Liver-function tests.—Plasma-bilirubin 5·8 mg. per 100 ml.—mostly direct reacting. Total plasma-proteins 8·3 g. per 100 ml. (electrophoretic analysis: albumin, 33%; globulins, α_1 6%, α_2 10%, β 17%, and γ 34%). Prothrombin concentration 100%. Thymol turbidity 7 u. Cephalin cholesterol flocculation + at 48 hours. Alkaline phosphatase 64 King-Armstrong units per 100 ml. Urine contained bile pigment.

Fæces.—Fat 9·7 g. per day. Nitrogen 1·6 g. per day. Digitonin-precipitable sterol 850 mg. per day. Colour normal.

Biopsies.—Liver showed some periportal fibrosis and dilatation of bile canaliculi. A skin lesion showed collagen destruction and numerous foam cells but no Touton giant cells.

X-rays.—No evidence of gallstones, œsophageal varices, osteomalacia, or pulmonary disease.

Hæmatology.—Hæmoglobin 12·5 g. per 100 ml. White cells 8700 with normal differential count.

Treatment

A 2200-calorie, liquid, formula diet containing 40 g. ethyl linoleate, 97 g. protein, and 362 g. carbohydrate was started on Feb. 10. The ethyl linoleate was increased to 80 g. daily on Feb. 17, and to 120 g. on March 3. The latter dose caused intestinal hurry and was reduced to 80 g. daily on March 15. The calorie and protein intakes were constant throughout and changes in ethyl linoleate were balanced by changes in carbohydrate intake. On April 14 the diet was changed to 400 g. ' Saf-Lac ' (non-fat milk solids with 40% safflower oil) providing 160 g. fat (110 g. linoleic acid), 84 g. protein, 124 g. carbohydrate, and 2270 calories. Fruit, vegetables, and cereals were added later. She was discharged home on May 4, and remained on the same diet thereafter.

Progress

The dramatic and sustained fall in the plasma level of total lipids, cholesterol, and phospholipids is shown in fig. 1. Plasma alkaline phosphatase and cholate levels are shown in the table with the cholesterol-ester fatty acid iodine values and

EFFECTS OF TREATMENT

Date	Stage of treatment	Cholesterol-ester fatty acid		Plasma-cholate (μg. per ml.)		Alkaline phosphatase
		Iodine value	% Dienoic acid	Di-hydroxy-	Tri-hydroxy-	King-Armstrong units
Feb. 5	Before	112	22	..	..	..
Feb. 9	Before	112	25	..	..	64
Feb. 10	1st day	113	25	35·7	33·6	..
Feb. 26	3rd week	129	40	70·7	59·5	58
March 21	6th week	145	59	38·6	8·7	70
April 30	12th week	151	62	60·3	34·5	49
May 21	16th week	..	..	12·6	6·8	..
June 14	19th week	..	..	21·2	3·8	..
Sept. 20	32nd week	..	..	20·3	13·0	48
Normal range ..		114–150	33–58	1·8–4·7	2·8–4·7	3·0–13
Mean		131	45	3·1	4·8	8

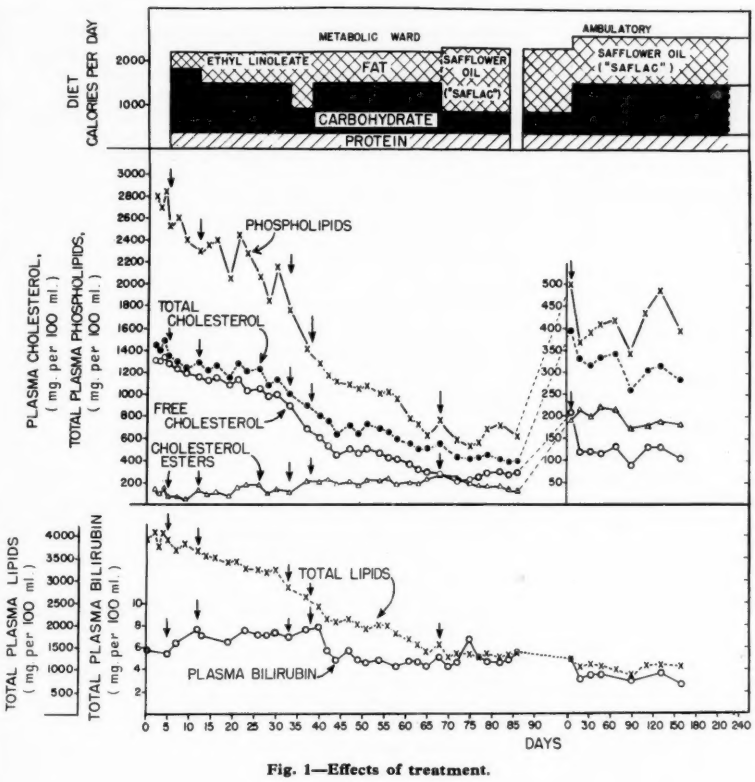


Fig. 1—Effects of treatment.

dienoic-acid concentrations. Within 2 months of starting treatment some of the smaller xanthomata had disappeared and the larger ones were becoming smaller. Scleral jaundice was less and the skin was much less dry and pigmented. Subsequent disappearance of the xanthomata was rapid, and 9 months after starting treatment all but the larger lesions had disappeared (fig. 2). The pruritus became less intense but did not clear completely. Subjective improvement was considerable, and within 2 months of discharge the patient was able to do all her own housework, whereas during the 3 months before admission she had spent most of her time in bed.

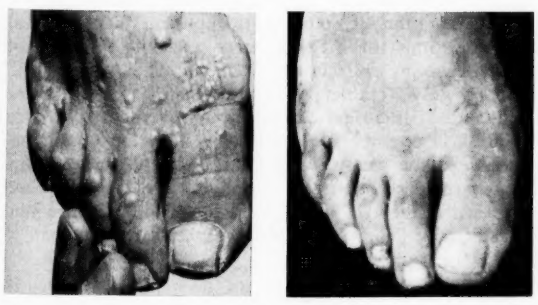
Discussion

Hitherto, no drug or diet has been found to have a sustained effect on the biochemical and clinical abnormalities of primary biliary cirrhosis. Periportal fibrosis increases slowly, and death from liver failure or from hæmorrhage from œsophageal varices usually occurs within 3–6 years of the onset of symptoms. Ahrens et al. (1950) have shown that in the late stages the plasma-lipid level falls and the xanthomata disappear. It was therefore expected that the xanthomata would disappear in our patient as the plasma-lipid level fell. It is not known whether the high plasma-lipid level contributes to the development of cirrhosis, and whether lowering the level will alter the course of the liver changes.

The disparity between the behaviour of free and esterified cholesterol is striking. The ester/free ratio of normal plasma is approximately 2. In our patient the initial value was 0·11. The marked fall of plasma-cholesterol during treatment was confined to the free fraction: the ester level rose slightly. On Oct. 18, 35 weeks after starting treatment, the ratio was 1·73. The free-cholesterol and phospholipid levels fell together. A general parallelism between these lipids has been noticed by Smyrl in the blood of patients with many different diseases and with widely different absolute values. In extrahepatic obstructive jaundice, the plasma total cholesterol increases, and the ester/free ratio decreases, in proportion to the severity of the obstruction, as judged by the plasma-bilirubin (Zieve 1953). The fall in the ester fraction is generally attributed to liver-cell damage, which is supposed to impair esterification. In our patient, liver-cell function, assessed by conventional methods, was fairly good.

Pruritus, which is generally thought to be due to bile salt retention, was an early symptom and has persisted. The plasma-cholate level was initially about 10 times normal and after 8 months' treatment was still about 7 times normal.

The dienoic (largely linoleic) acid fraction of the plasma cholesterol-ester fatty acids was initially lower than normal but rose during treatment to levels seen in normal subjects studied under similar conditions. The significance of the low initial value is not clear.



a b

Fig. 2—Xanthomata (a) before and (b) after nine months treatment, showing disappearance of all but the largest.

'Saf-Lac' was provided through the courtesy of Dr. John Van Dolah of the Carnation Company, Los Angeles, California.

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COMA DUE TO MEPROBAMATE INTOXICATION

REPORT OF A CASE CONFIRMED BY CHEMICAL ANALYSIS

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WHEN the tranquillising drug meprobamate (2 methyl, 2-N-propyl-1,3,-propanediol dicarbamate: 'Equanil', 'Miltown', 'Mepavlon', or 'Restenil') was introduced it was thought (Selling 1955) that large amounts could be taken without serious ill effects. That this might not always be so was suggested by the varying effects of therapeutic dosage observed by Borrus (1955); marked drowsiness was produced in some patients while others having similar doses noticed none. Since then a few cases of coma from attempted suicide with meprobamate have been reported. In these the diagnosis has usually been suggested by finding the drug in the patient's possession, and it has always been confirmed by the patient's admission of overdosage. Chemical tests were not used to prove the diagnosis. The following case of meprobamate intoxication is of interest because the clinical features were unusual and because chemical analysis showed that, contrary to the patient's statement, an overdose had been taken.

Case-report

A merchant seaman, aged 27, was admitted on Nov. 30, 1957, to The London Hospital (no. 36552/57). He was admitted at 8 P.M. from an East End café where he had lost consciousness after drinking a cup of tea. All that was known of him was discovered from the contents of his pockets, which included his merchant seaman's identity book and one white tablet. Unfortunately the latter was broken and the proprietary name (probably either 'Restenil' or 'Restenyl') was incomplete.

Examination

A well-built young man, responding only slowly to painful stimuli; face flushed, generalised cutaneous vasodilatation; oral temperature 98·4°F, pulse-rate 80, and blood-pressure 95/70 mm. Hg; respirations a little rapid (24 per minute), movements not unduly shallow, no cyanosis. Nothing significant found in the chest or abdomen, where there was the scar of an old upper right paramedian incision; no neck stiffness; corneal and eyelash reflexes absent, pupils equal, normal in size, and reacting to light; limbs at times flaccid, at others showing variable resistance to passive movements; tendon reflexes present but depressed, plantar responses flexor.

Catheterisation yielded only 8 ml. of urine which was normal to routine testing, and gave no special colour with ferric chloride.

Management and Progress

Gastric aspiration produced a small volume of yellow fluid. Neither this nor gastric washings had any particular odour, and each gave a negative test with ferric chloride. Blood-sugar 95 mg. per 100 ml.

The coma deepened slightly, and response to painful stimuli became barely perceptible. An intravenous injection of nikethamide 5 ml. produced transient improvement and a short burst of violent sneezing. During the night the blood-pressure fell gradually to 50 mm. Hg at 7 A.M. There was little tachycardia, and cutaneous vasodilatation was still very conspicuous. A rise in blood-pressure following intramuscular and intravenous injection of methylamphetamine was poorly sustained; an intravenous infusion of noradrenaline ('Levophed') in 5% dextrose solution was therefore given, and kept the systolic pressure around 100 mm. Hg. Further analeptic drugs were not given in view of the uncertain diagnosis. The condition remained unchanged clinically. The tendon reflexes were never lost, and the pupils continued to react to light. An additional feature was a shivering response each time he was exposed to cold by turning back the bedclothes.

He began to improve 37 hours after admission. There was then a gradual increase in his responses, and 2 hours later he replied to spoken commands. The deep reflexes improved, and the blood-pressure rose. At this stage, despite an intravenous intake of nearly 2 litres of 5% dextrose solution, he had not passed urine; catheterisation yielded 230 ml. of concentrated urine, and a rapid diuresis with incontinence followed almost immediately. From this point progress was uneventful.

Investigations

While he was in coma the following investigations were made with negative results: lumbar puncture and analysis of the cerebrospinal fluid, estimation of blood-urea and serum-electrolytes, and estimation of the blood-barbiturate content. Specimens of the gastric contents and washings, of blood taken at 11 P.M. on Nov. 30, and of the urine obtained by catheterisation at the end of his coma were saved for analysis.

After he had recovered it was learnt that 'Restenil' is a Scandinavian preparation of meprobamate, and that 20 tablets (each of 400 mg.) had been prescribed for the patient in Bergen 12 days previously. The patient said he had received about 50 tablets, which he claimed to have taken three times a day as directed; he repeatedly denied having taken an overdose.

Comment

From the outset this case was unusual, and when the more common causes of coma had been excluded the diagnosis seemed to lie between some rare form of chemical intoxication and hysteria. But the development of severe hypotension and oliguria, and the sequence of events during recovery excluded hysteria. It was assumed that he had taken an overdose of restenil and that this was one of the modern tranquillising drugs. Reference to pharmaceutical data later showed that this preparation contained meprobamate.

The published records of seven cases of coma due to meprobamate (Charet et al. 1956, Collins-Dineen 1956, Hiestand 1956, Heberden and Cooper 1957, Woodward 1957) all describe profound coma, with absent tendon and pupillary reflexes. Prolonged semi-coma with preservation of these reflexes has not been described. Although a mild fall in blood-pressure was usual, only Woodward (1957) found hypotension of the degree recorded in this case. Woodward's patient remained in deep coma for 44 hours after 96 tablets (38·4 g.), and the systolic blood-pressure fell to 40 mm. Hg. Woodward refers to another case developing shock with a blood-pressure of 70/40 mm. Hg. The combination of hypotension and conspicuous cutaneous vasodilatation without shock appears to be more characteristic of meprobamate intoxication.

The duration of coma in this patient is of interest because, from the little evidence available (Woodward 1957), it seems unlikely that coma would have lasted 37 hours if only 20 tablets of meprobamate had been taken. When the patient refused to admit overdosage, it was decided to attempt a quantitative estimation of meprobamate in the gastric contents, blood, and urine. This was particularly desirable since in this case, in contrast with other recorded cases, the blood-pressure was considerably depressed in the absence of deep coma.

Chemical Investigation

Method

A method of estimating meprobamate in biological fluids was described by Agranoff et al. (1957) who studied its urinary excretion. Meprobamate was extracted with ether at an alkaline pH, and after evaporation of the ether it was heated

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with concentrated sulphuric acid and estimated from the peak of absorption which it gave at 450 mμ. In this investigation the peak has been found consistently at 440 mμ. With a minor alteration on this account, their method has been used to estimate meprobamate in both urine and gastric contents. In addition, estimations were made in parallel on the patient's blood and on control blood (from a subject who had not taken meprobamate) to which various known amounts of meprobamate had been added. Concentrations equivalent to 0, 10, 20, and 30 mg. per 100 ml. provided a suitable range from which a straight-line curve was drawn, and from this the concentration in the test blood was obtained. In the procedure used, details of which are given below, the proteins were first precipitated from whole blood with tungstic acid. Estimations were made on 1 ml. of blood, and the meprobamate was added in aqueous solution before the proteins were precipitated. Estimations were made in duplicate for each sample of blood, and the mean value was taken.

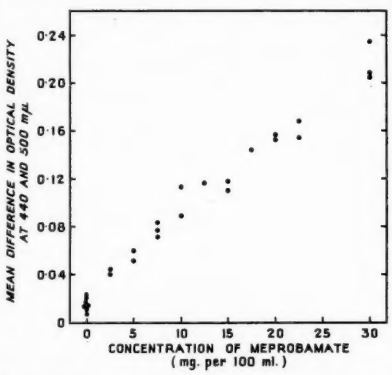

Fig. 1—Analysis of results of estimation of known amounts of meprobamate added to seven samples of normal blood.

Procedure

1 ml. of the blood sample, 5 ml. of distilled water, 1 ml. of 10% sodium tungstate solution, and 1 ml. of 2/3 *N* sulphuric acid are placed in a centrifuge tube and mixed by repeated inversion. After centrifugation, 5 ml. of the clear supernatant fluid is removed and extracted with 9 ml. of ether. (The addition of sodium hydroxide to produce an alkaline pH makes no appreciable difference and has been omitted.) 7 ml. of the ether phase is removed and evaporated to dryness in a clean tube. 1 ml. of concentrated sulphuric acid is added, and the tube is heated at 100°C for 30 minutes. After cooling, 2 ml. of distilled water is added slowly. 15 minutes later, the optical densities at 440 mμ and 500 mμ are measured against a water blank to give a value of the difference in density at the two wavelengths.

Results

A concentration of 2·7 mg. per ml., representing a total of 621 mg. in the original 230 ml. specimen, was found in the urine. In the gastric contents and washings the concentrations were 4·7 mg. per ml. and 0·21 mg. per ml. respectively, but since the volumes of these specimens were not recorded the total amount recovered from the stomach is not known.

TABLE I—COMPARISON OF MEPROBAMATE AND THE SUBSTANCE IN THE PATIENT'S URINE IN THEIR DISTRIBUTION BETWEEN MIXTURES OF EQUAL VOLUMES OF ALKALINE URINE AND VARIOUS ORGANIC SOLVENTS

Solvent	Pure meprobamate	Patient's urinary "meprobamate"
Ether	0·73	0·75
Benzene	0·24	0·21
Heptane	0·16	0·14
Ethylene dichloride	0·57	0·65

The value given is the fraction recovered in the organic solvent.

A concentration of 21·5 mg. per 100 ml. was found in the patient's blood; levels of 0·8 and 2·1 mg. per 100 ml. were found in two normal subjects 3 hours after an oral dose of 1600 mg. The accuracy of the estimation in blood has not been examined statistically, but fig. 1 shows that no gross error is introduced by using different blood as a control. The results of estimations on seven samples of normal blood, to which various known amounts of meprobamate were added, are amalgamated and show a general linear correlation with lack of marked scatter.

In an attempt to establish that the substance estimated was meprobamate, the following steps were taken:

(1) The complete absorption curves (over the range 380–600 mμ) of the test and control solutions were recorded after the estimations had been made. The similarity of these curves for urine and blood is apparent from figs. 2 and 3.

TABLE II—DETAILS OF PAPER CHROMATOGRAPHY AND R_F VALUES FOR MEPROBAMATE

Solvent system	Meprobamate R_F value	Approx. time of development (hr.)
60% methanol	0·81	5
85% *n*-butanol	0·67	32
70% ethanol	0·76	7
Pyridine/water (65/35 v/v)	0·76	8
80% *n*-propanol	0·78	15

(2) Comparative distribution ratios were determined for meprobamate added to urine and for the unknown substance in urine. The procedure used by Agranoff et al. (1957) was followed, and the values recorded in table I correspond closely.

(3) Independent evidence of the identity of the meprobamate in the urine was obtained by paper chromatography. Mobilities of known and unknown were compared in a number of solvent systems, and in each system a mixture of the two moved as one spot. The solvent systems used, the R_F values of meprobamate in each, and the approximate times of development are listed in table II. Strict quantitative methods were not used but the results agreed with the value given by the chemical method of estimation. For technical reasons it was not possible to use paper chromatography to identify meprobamate in blood.

Unidirectional chromatograms employing downward development on Whatman no. 1 filterpaper were used. The material was applied in alcoholic solution, and amounts containing between 25 and 50 μg. gave spots of a suitable size. The meprobamate was first extracted from the urine with ether and then redissolved in alcohol. Development in each system was allowed to proceed until a distance of more than 30 cm. had been covered by the solvent front. After drying in air, the spots were located by spraying in turn with 1% sodium hypochlorite solution, ethyl alcohol, and a mixture of equal volumes of 1% starch and *M*/20 potassium iodide. I am indebted to Dr. T. H. Farmer for the suggestion that this method (Pan and Dutcher 1956) would detect meprobamate.

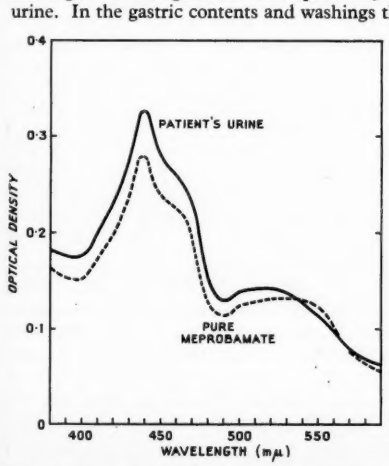

Fig. 2—Absorption curves from estimation in urine.

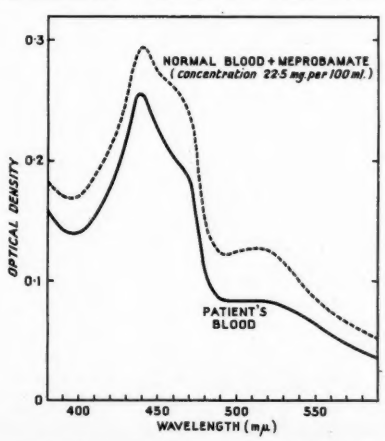

Fig. 3—Absorption curves from estimation in blood.

Discussion

There can be little doubt that meprobamate was present in the various specimens; but, since the patient claimed to have taken the drug only in therapeutic amounts, the figures must be examined to determine whether he had taken an overdose. The finding of a blood-level of 21·5 mg. per 100 ml., compared with the control values after ingestion of 1600 mg., is by itself sufficient for this purpose. The large amount recovered from the urine is also strongly suggestive, for Agranoff et al. (1957) found that only 10–20% of an oral dose of 1600 mg. was recovered from the urine during the first 24 hours. In this patient the urine volume was greatly reduced, presumably because of the severe hypotension. Despite the fact that only 230 ml. of urine was obtained over a 36-hour period, 621 mg. of meprobamate was recovered. This is not compatible with the ingestion of 400 mg. three times a day, which the patient claimed.

In cases where the diagnosis is in doubt, an estimation of meprobamate in the blood, although rather laborious, would provide a more certain answer than the examination of either urine or gastric contents. But the concentration of meprobamate in the cerebrospinal fluid is probably only slightly lower than that in the blood. If this is so, an estimation on cerebrospinal fluid would be the method of choice, since, in a preliminary investigation, it has been found that meprobamate added to this fluid can be estimated directly by the method used for urine.

In this case the specimens had been stored for up to 8 months at 4°C before they were analysed.

An observation of some interest was made in the subjects who were given 1600 mg. of meprobamate by mouth. The one with the lower blood-level (0·8 mg. per 100 ml.) noticed no ill effects, but the other (2·1 mg. per 100 ml.) became extremely sleepy and for 5–6 hours was difficult to rouse. This variation in response, and its possible correlation with the blood-level, has not been further investigated, because it was felt that the present method of estimating blood-levels is not sufficiently sensitive.

Summary

A case of meprobamate intoxication is described. The chief clinical features were a prolonged state of semi-coma, cutaneous vasodilatation, hypotension, and reduction of urinary output.

Chemical estimation of meprobamate in the gastric contents, blood, and urine was used to confirm the diagnosis of overdosage. A method of estimating meprobamate in blood is described.

I am grateful to Prof. Clifford Wilson, who gave permission for this case to be published, Prof. C. J. O. R. Morris, and Dr. J. T. Wright for their help and encouragement. To John Wyeth & Brother Ltd. I am indebted for a supply of pure meprobamate.

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Addendum

Since this paper was written, further cases of meprobamate intoxication have been reported. Powell et al. (1958) describe two cases of suicide in which meprobamate was detected in the specimens of liver, urine, and stomach-content taken at necropsy. The methods of analysis were not recorded.

A number of reactions by which meprobamate may be estimated have now been suggested. These are reviewed by Walkenstein et al. (1958), who have developed a sensitive method of estimating the substance in plasma. They found that, in dogs given an oral dose of 90 mg. per kg., the plasma-level reached a maximum of 4·5 mg. per 100 ml. after 2 hours. This further supports the conclusion that the blood-level of 21·5 mg. per 100 ml. recorded in this patient resulted from an overdose. Since their method gives high blank values with whole blood, it may not be as sensitive when only hæmolysed specimens are available, as in the present instance.

Techniques of detecting meprobamate on paper chromatograms, similar to that used in this study, have also been used by Walkenstein et al. (1958) and by Curry (1959) who reported this at a London meeting of the Association of Clinical Biochemists in June, 1957.

Curry, A. S. (1959) personal communication.
Powell, L. W., Mann, G. T., Kaye, S. (1958) *New Engl. J. Med.* **259**, 716.
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Medical Societies

MANCHESTER MEDICAL SOCIETY

Testicular Biopsy

AT a meeting of the section of pathology on Dec. 10, Dr. B. SANDLER said that testicular biopsy gives more information about spermatogenesis than semen analysis and can be of value in prognosis and sometimes in deciding the type of treatment. He prefers the punch-biopsy technique and described six main conditions that can be recognised:

(1) *Normal spermatogenesis* may be found when there is azoospermia due to duct obstruction. Absence of seminal fructose indicates that the obstruction is blocking the vesicles. These cases are amenable to surgical exploration provided the congenital defect is confined to the vasa and does not affect the testes and epididymis as well.

(2) *Eunuchoidism*, which is rarely encountered in infertility clinics.

(3) *Hypospermatogenesis*, which is quite commonly present after any severe illness and often in the presence of toxic infections such as teeth and sinus infections, may be produced by protracted administration of œstrogens.

(4) In *germinal aplasia* with incurable azoospermia, spermatogenesis is not present at all, similar appearances being encountered after exposure to radioactive agents and factors.

(5) *Progressive tubular degeneration* is a common condition always associated with Leydig-cell hyperplasia—a progressive condition which, after some years, ends in azoospermia. These cases should be recognised early so that adequate treatment may be given to the wife to render her fully fertile and a conception obtained before the husband becomes finally sterile.

(6) *Spermatogenic arrest* occurs quite often in men under the age of 30 and can take place at the spermatid, spermatocyte, or spermatogonia stage. The constancy of the point of arrest is in contrast to the variability seen in other conditions, and no treatment has any effect in such cases.

No correlation has been found between the biopsy appearances and the seminal analyses, or between either of these and urinary excretion of hormones. In most cases of male sterility there is no effective treatment, but early investigation of both partners may reveal early cases of progressive tubular atrophy before azoospermia has developed, and treatment of the wife's hostile cervical mucus may enable conception to occur. In the majority of cases, however, a testicular condition will be found for which no treatment is possible at present.

Reviews of Books

Diffuse Lesions of the Stomach

IAN J. WOOD, M.D. Melb., F.R.C.P., F.R.A.C.P., head of the clinical research unit of the Royal Melbourne Hospital and the Walter and Eliza Hall Institute; LEON I. TAFT, M.B., B.SC. Melb., pathologist to the clinical research unit, Melbourne, Australia. London: Edward Arnold. 1958. Pp. 86. 24*s*.

Sir Macfarlane Burnet, founder of the research unit whence this modest but important monograph emanates, used to tell the authors that new knowledge often followed closely in the wake of new technique. The new technique in this case was gastric biopsy, performed with the Hermon Taylor gastroscope, the Benedict operating gastroscope, or the flexible instrument designed and perfected by the authors themselves.

Chronic gastritis used to be a favourite diagnosis; and its abuse may have been largely responsible for its disrepute. Necropsy reports of diffuse chronic inflammation of the gastric mucosa could be criticised on the ground that similar changes were caused by autodigestion; and from here it was but a short false step (and false steps are notoriously short) to assert that chronic inflammation hardly existed at all. This view prevailed—though it was never shared by old-fashioned family doctors—until challenged by Faber, Schindler, and, most decisively, the Australian team.

The Melbourne workers distinguish several types of chronic gastritis—superficial, atrophic, giant hypertrophic, and extreme atrophic in pernicious anæmia—and they have demonstrated corresponding histological changes in the live gastric mucosa. They suggest that, with the requisite patience, sympathy, and knowledge, the symptoms and signs of chronic gastritis are as distinctive as the histological lesions.

The ætiology of chronic gastritis—and its degree of kinship to gastric and duodenal ulcer, gastrointestinal cancer, and the various anæmias—remains a mystery, but with shafts of light piercing the darkness. Dr. Wood and Dr. Taft have resisted all temptation to present intelligent guesswork as proven fact. Such uncommon restraint will reap its reward by tempting readers to venture into the darkness themselves. None can afford to ignore chronic gastric disorders; and they are a field for investigation where acute observation and inspired thinking are still infinitely more useful than elaborate technical apparatus. It would be interesting to know, for instance, why alkalis relieve the pain in a condition of which achlorhydria is a cardinal feature.

Modern Trends in Surgical Materials

Editor: LEON GILLIS, M.B.E., M.CH. ORTH., F.R.C.S., consultant surgeon, Queen Mary's Hospital, Roehampton. London: Butterworth. 1958. Pp. 275. 72*s*. 6*d*.

EMPIRICISM has long dominated the surgeon's choice of materials. How otherwise? For he must get on with the job; and few have the time, aptitude, or interest to delve into, for example, the mysteries of metallurgy or the physics of plastics. It comes as a surprise, therefore, that nothing quite like this book has been published before, because it meets an obvious need.

The work opens with a clear explanation of metal corrosion by a physicist, and there follow a discussion of the reaction of tissue to metal and alloys, cytotoxicity, and carcinogenicity by two veterinary surgeons; further adumbrations from physicists; a review of the use and pathological effects of metals in surgery; and two chapters by surgeons, proved by their words to be masters of their subject. And so to plastics. The editor can rightly claim that new ground has been covered in a chapter on biomechanics, which immediately follows one in which the pros and cons of implant materials of all kinds are discussed. Materials with which most of us are familiar, such as catgut and the simple rubber drainage tube, have not been overlooked. Grafts of all types—skin, corneal, arterial, and bone—find a place, with instructions regarding storage. Splintage, prosthetics (including dental), and appliances are all to be found, with a final chapter on sterilisation.

This volume is authoritative and is unusual in that, though a work of reference, it is readable. Reading it imparts the feeling that we are only on the fringe of the surgery of conservation.

Urology in Outline

T. L. CHAPMAN, CH.M., F.R.C.S., F.R.F.P.S., urological surgeon, Victoria Infirmary, Glasgow, Hairmyres Hospital, Lanarkshire, and Ballochmyle Hospital, Ayrshire. Edinburgh: E. & S. Livingstone. 1958. Pp. 176. 27*s*. 6*d*.

This diagrammatic atlas of urology will appeal particularly to those gifted with a retentive memory for visual impressions who wish to acquaint themselves rapidly with the broad outlines of the specialty. The advances of recent years in urological diagnosis and treatment and in the understanding of physiological function and fluid balance have been considerable, yet many students complete their surgical studies with only a transient and inadequate experience of the subject. For them the profusion of simple illustrations and the brief explanatory text will be a means of extending their knowledge with barely perceptible effort and a guide to rapid revision. The system of instruction is very like a series of animated cartoons, each dealing with one aspect of urological disease and its management. In general, technical details are rigorously excluded and the important features are indicated in simple diagrams which usually convey an immediate meaning. Almost every page reveals information of direct practical value, though a few of the illustrations are marred by their diminutive size. We warmly recommend this literal synopsis to all students with an eye to improving their knowledge of this important subject.

Cancer

Vols. III and IV. Editor: RONALD W. RAVEN, O.B.E., F.R.C.S., surgeon, Royal Marsden Hospital and French Hospital. London: Butterworth. 1958. Vol. III, pp. 501; vol. IV, pp. 555. 85*s*. each.

THE first two volumes [1] of this System of Cancer dealt with research into the causation of cancer and with the pathology of human tumours.

Vol. III is a mixed bag of five sections: pathological aspects geography of cancer, occupational cancer, cancer education, and cancer detection. The pathology section is up to date, well written, and informative. The geography of cancer is inevitably dealt with somewhat incompletely, as information of any value is limited to certain countries where adequate statistics are available.

Vol. IV is concerned entirely with clinical aspects. Apart from a general chapter on " staging ", the book is devoted to malignant tumours by anatomical regions in 33 chapters written by various surgeons. Unhappily the writers seem not to have decided on the audience they wish to address. The result is that this volume seems too elementary for the practising surgeon, yet too narrow for the physician, and likely to be of little value to the general practitioner.

Obstetrics and Gynæcology

J. R. WILLSON, professor and head of department of obstetrics and gynecology; C. T. BEECHAM, clinical professor of obstetrics and gynecology; I. FORMAN, clinical professor of obstetrics and gynecology; E. R. CARRINGTON, assistant professor of obstetrics and gynecology; Temple University Medical Center. Philadelphia, Pa. London: Henry Kimpton. 1958. Pp. 605. 80*s*.

THIS combined book of obstetrics and gynæcology has grown out of a repeatedly revised series of lectures to students. The ground is well covered except for operative and manipulative details, which the authors feel would be of more interest to practising clinicians. An attempt has been made to integrate obstetrics with gynæcology by sandwiching the former, halfway through the patient's life and halfway in the book, between (rather arbitrarily) the chapters on endometriosis and benign lesions of the cervix, with pædiatric gynæcology and the uses of the sex hormones tucked in near the end. The objective is clearly to picture the patient's medical life-history and hazards as a sequential whole. In this the work fails in so far as a woman's life, mercifully, extends beyond the narrow confines of gynæcology and obstetrics.

1. See *Lancet* 1958, i. 1003.

The book is weakest on the practical aspects of midwifery, and it is a pity that subjects such as resuscitation of the newborn and the management of prematurity have been curtailed—probably in the mistaken view that these matters interest pædiatricians only. Nevertheless the volume contains much that is pleasing and thoroughly up to date. Any amount of outspoken common sense shines through its pages. If this is the intellectual fare of undergraduates at Temple University they certainly have cause to value their teachers.

Peripheral Nerve Injuries

RUTH E. M. BOWDEN, D.SC., M.B., professor of anatomy, Royal Free Hospital School of Medicine, University of London. London: H. K. Lewis. 1958. Pp. 62. 8*s*. 6*d*.

INJURIES to peripheral nerves are common in war; but important experience then gained in their management is too easily forgotten when the war is over. This small book is based on Professor Bowden's experience of war-injured patients and is intended to instruct physiotherapists, medical students, and housemen, and to be an aide-memoire to their seniors. It is particularly valuable in putting forward the principles of diagnosis, classification, and treatment clearly and in small compass, and in stating the daily activities which may be hindered by various injuries. In further editions the inclusion of a section on the peripheral-nerve injuries commonly seen in civilian neurological practice might add to the appeal of this work.

Recent Advances in Pædiatrics (2nd ed. London: J. & A. Churchill. 1958. Pp. 378. 48*s*.).—A book on recent advances in pædiatrics which excludes psychology, sociology, genetics, and neoplasia, and includes tuberculosis and rheumatic fever must, at first sight, seem unbalanced. Though the selection of material may be questioned, the quality of the contents is uniformly excellent. Perhaps the outstanding feature of this edition is the space devoted to fundamentals. Dawes on fœtal and neonatal physiology, Lathe on bilirubin metabolism, Gairdner on hæmatology, and Hutchison on the thyroid form an exciting constellation which makes the sections on clinical topics seem almost pedestrian. Mcnab has some real progress to report in the treatment of spina bifida cystica and hydrocephalus; and modern knowledge of the nephrotic syndrome, tuberculosis, rheumatic fever, and pyogenic osteitis is admirably summarised. The finer points and possible scope of pædiatric anthropometry are ably discussed by Falkner, and Miss Edith Whetnall has written an excellent review of deafness in childhood. This book, edited by Dr. Douglas Gairdner, is absolutely up to date, but has none of the evanescence of a yearbook. The subjects are fully discussed and new work thoughtfully evaluated. This is a book to buy, not to borrow.

Psycho-analysis and Contemporary Thought (Vol. 53, International Psycho-analytical Library. London: Hogarth Press. 1958. Pp. 149. 25*s*.).—This book, edited by Dr. J. D. Sutherland, gives the text of six public lectures delivered by members of the British Psycho-Analytical Society in 1956 as part of the celebrations of the centenary of Freud's birth. The order of the lectures has been changed for publication. Dr. D. W. Winnicott's paper on psychoanalysis and the sense of guilt comes first, followed by two papers concerned with Care by Dr. John Bowlby, and Psychoanalysis and the Teacher by Dr. Ilse Hellman. The papers on Psychoanalysis and Art by Dr. Marion Milner, Psychoanalysis and Philosophy by Mrs. Roger Money-Kyrle, and Psychoanalysis and the Current Economic Crisis by Dr. E. Jaques, illustrate the wide range of contemporary affairs to which psychoanalysts are giving their attention. A brief paper on a character trait of Freud's, by Mrs. J. Riviere, concludes the book.

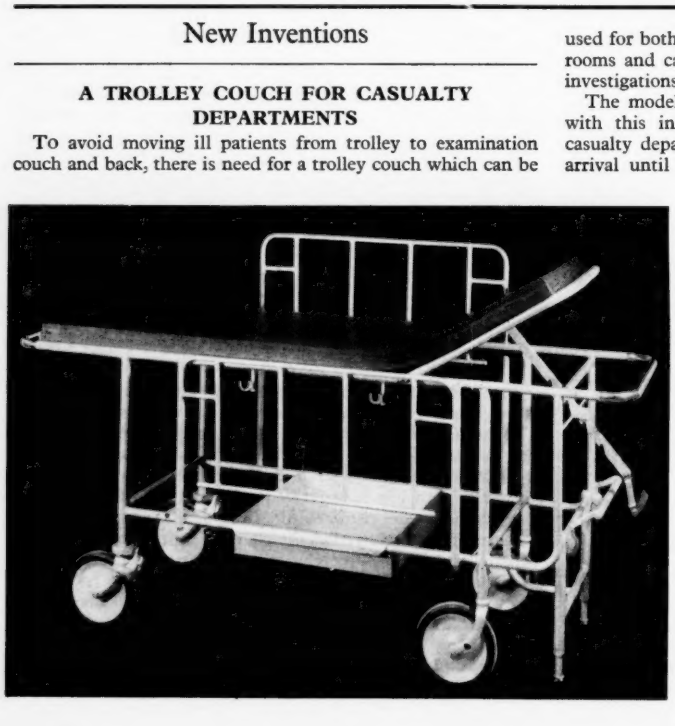
Physiotherapy in Chest Diseases (London: Chest and Heart Association. 1958. Pp. 98. 12*s*. 6*d*.).—This booklet by Dr. Torsten Bruce, Caroline Reutersward, and Birgit Westin describes the physiotherapeutic techniques in chest surgery practised at Söderby Hospital, Uttran, Sweden. After a short description of the relevant chest conditions by Dr. Bruce, the various treatments are simply and clearly explained by his two co-authors, who are physiotherapists. Particular attention is devoted to thoracoplasty; but the methods described are applicable in many instances to other operative procedures, including resection for non-tuberculous chest disease. The illustrations are clear and helpful. The need for cooperation with the medical and nursing staff is sensibly recognised.

New Inventions

A TROLLEY COUCH FOR CASUALTY DEPARTMENTS

To avoid moving ill patients from trolley to examination couch and back, there is need for a trolley couch which can be used for both purposes in casualty departments and receiving-rooms and can take the patient to be X-rayed or have other investigations.

The model now in use in this hospital has been designed with this in mind. A recumbent patient brought to the casualty department remains on this couch from the time of arrival until he is either admitted or sent home. Its chief features are:



1. Full swivelling of all four wheels with pedal brakes and 'Homa' castors, and a 'Cam' stabiliser at the head, raising it off the ground when it is in use as a static couch.
2. Cot sides which can be raised and locked for a restless or unconscious patient.
3. An easily movable ratchet adjustment for raising and lowering the head.
4. A metal tray for carrying the patient's luggage and clothes.
5. A mattress made of sponge rubber 2-in. thick. A metal retaining strip at the foot prevents this from slipping.

This trolley couch has now been used for some months and has proved entirely satisfactory. It is made to our design by Phillips Ltd., Excelsior Works, Birmingham 18.

D. G. H. SYLVESTER
M.D. Lond.
Resident Medical Officer
The Middlesex Hospital, London, W.1

THE LANCET

LONDON 7 FEBRUARY 1959

Treatment of a Stroke

IN the past, management of a patient who had suffered a "stroke" presented no problem: the physician's choice lay between masterly inactivity and skilful neglect. The position now is different and more difficult. We are at an awkward intermediate stage half way towards understanding of the factors involved. With anticoagulants and enzymes such as fibrinolysin, with hypotensive drugs, with increased knowledge of cardiac physiology, with hypothermia, and with a few successful ventures in surgical treatment behind us, the physician can no longer be sure that advice to do nothing is the best he can offer. No one form of treatment should be considered in isolation. A stroke is a single incident in the progress of a generalised disease which may be atheroma, arteriosclerosis, hypertension, or a thromboembolic proclivity.

WRIGHT [1] points out that both general and local factors must be taken into account. Whereas disease of the heart leading to embolism accounts for a small proportion of the cases, in a large majority the underlying causes are still obscure. The effects of the level of cholesterol in blood, of diet and exercise, and even of ordinary movement of the artery itself are unknown. Local factors include permanent changes in the wall of the vessel and temporary disorders of the blood and plasma within them. The physical state of particles in the blood, the adhesiveness of their surfaces, the charges of colloid, and chemical equilibrium between enzymes are all believed to play a part. A chain of reactions is thought to lead to the production of a sufficient concentration of thrombin to convert fibrinogen to fibrin; but even the crudest simplification of the postulated reaction includes eight stages. Each stage has its inhibitors as well as its activators; minor changes in platelets may lead to escape of some of their contents, so that they become covered with a film of fibrin which has such viscosity that particles begin to adhere even though they have a like electric charge.[2–5] Some believe that both the wall of the artery and fibrinogen have negative charges, leading to mutual repulsion but that these charges are reduced by hydrophilic colloids, which are increased in blood postoperatively, and which modify the positions of absorbed water on cell surfaces. Such hydrophilic colloids include fibrinogen itself and globulin. In cases of stroke the possibility of such diseases as malignant tumour or a primary disorder of the circulating blood should be borne in mind.

Cerebral hæmorrhage is not, as some once believed, necessarily fatal. Numerous small hæmorrhages are seen at necropsy, both in the conditions already named and after injury. Occlusion of an artery of the brain may lead to an infarct into which hæmorrhage may occur. Some aneurysms, whatever they may have been originally, are obviously false aneurysms by the time they are seen at operation or necropsy. Hæmorrhages from angiomas are even less liable to cause immediate death and must therefore be remembered in seeking the cause of a stroke. Basilar or carotid artery thrombosis may give rise to a characteristic picture,[6] but on the other hand may cause deprivation of blood so far from their immediate distribution that diagnosis is impossible without angiography.

If the blood-pressure is normal and the cerebrospinal fluid clear, if there is a previous history suggestive of arterial occlusive disease, and if there are no symptoms or signs suggesting raised intracranial pressure, the case for the use of anticoagulants is strong; yet their administration is never free from risk, and they are probably best given orally, by which route they take some time to act. The exhibition of hypotensive drugs if the pressure is high also requires care but apparently benefits some cases; for the mere presence of a very high pressure may induce local constriction of the vessels. Methods calculated to act specifically on the cerebral circulation have their particular difficulties. The administration of carbon dioxide has been advocated. It increases the cerebral blood-flow; but its action is temporary, it tends to raise the intracranial pressure, and its effect on the coagulating factors in the blood is unknown. Temporary blocking of the stellate ganglion has proved disappointing, but surgical section of the cervical sympathetic trunk has occasionally led to steady improvement in borderline cases of cerebral ischæmia; as a general rule no dramatic effect ensues. The surgical treatment of aneurysms and of angiomas is occasionally mandatory; but in a large proportion of cases the benefits of active, as opposed to conservative, treatment are more equivocal, while in many cases (particularly in the elderly) direct surgical approach is impossible. The removal of intracerebral hæmatoma has also occasionally proved its worth.

Thrombosis of the internal carotid artery has been successfully treated by thrombendarterectomy, resection and anastomosis, or arterectomy.[7] An interesting development is described by DEBAKEY et al.[8] and LYONS and GALBRAITH,[9] who have treated partial or segmental occlusion of the carotid artery by means of synthetic grafts—a method that may prove especially valuable in the young. STEVENS [10] found that of 32 cases of "spontaneous" stroke in young patients, 16 were due to cerebral arterial thrombosis, and most of these were associated with a solitary atheromatous plaque. Endarterectomy with removal of the plaque,[11] or a grafting technique, may be undertaken. If this kind of surgery

1. Wright, I. S. *Ann. intern. Med.* 1958, **49**, 1004.
2. Apitz, K. *Virchows Arch. path. Anat.* 1942, **308**, 540.
3. Zucker, M. B. *Amer. J. Physiol.* 1947, **148**, 275.
4. Zucker, H. D. *Blood*, 1949, **4**, 631.
5. Wright, H. P. *in* Transactions of the Fourth Conference on Blood Clotting. New York, 1951.
6. Millikan, C. H., Siekert, R. C., Schick, R. M. *Proc. Mayo Clin.* 1955, **30**, 116, 578.
7. Rob, C., Wheeler, E. B. *Brit. med. J.* 1957, ii, 264.
8. DeBakey, M. E., Morris, G. C., Jordan, G. L., Cooley, D. A. *J. Amer. med. Ass.* 1958, **166**, 998.
9. Lyons, C., Galbraith, G. *Trans. Amer. Surg. Ass.* 1957, **75**, 183.
10. Stevens, H. *Ann. intern. Med.* 1958, **49**, 1022.
11. Cooley, D. A., Al-Naaman, Y. D., Corton, C. A. *J. Neurosurg.* 1956, **13** 500.

is to have a successful future, technical methods must take account of the fact that access to cerebral vessels is often obtained in the depths of a cleft, and that quite small vessels may be involved. The angle through which instruments can be moved may be only a few degrees, and if working parts have to be tiny they must be at the tip of a long instrument. End-to-end junction of small vessels with each other or with grafts cannot depend under such circumstances on some magical kind of manual dexterity: manœuvres must be brought within the range of normal movements of the hand. With the aid of perfusion the surgeon may be enabled to work in leisurely fashion with an empty segment or vessel. "When we look back," WRIGHT says, "to the state of heart surgery fifteen years ago and compare it with the present, we can feel encouraged and predict that, with increased interest and improved technics, vascular surgery of the brain will show great strides in the next decade." Such an advance will not be accomplished without blood, sweat, toil, and tears.

The "Floppy" Infant

IDENTIFYING the pathological change that underlies widespread hypotonia of the skeletal muscles in infants can be one of the most perplexing problems for the pædiatrician or neurologist. The late Dr. J. G. GREENFIELD spent the last few months of his life in the United States, where he worked on this question; and his work with colleagues at the National Institute of Neurological Diseases and Blindness, Bethesda, has now been reported.[1]

This group of workers suggest that cases of this nature fall into four principal groups, which vary considerably in prognosis: (1) infantile spinal muscular atrophy (Werdnig-Hoffmann disease), a progressive disorder which is eventually fatal [2 3]; (2) congenital muscular dystrophy [4 5], which is also progressive, though less rapidly so than spinal atrophy; (3) "central core disease",[6] in which the muscular weakness is stationary, neither progressing nor improving as the patient grows older; and (4) "benign congenital hypotonia",[7 8] in which there is steady improvement and eventual recovery. In their experience, muscle biopsy is the only really effective means of distinguishing between these disease entities or syndromes, and it may thus give information of the greatest prognostic value.

Patients with *infantile spinal muscular atrophy* have widespread weakness and hypotonia of the skeletal muscles. Usually the proximal limb muscles are affected first, but eventually weakness is generalised, the respiratory and pharyngeal muscles are involved, and fasciculation is seen in the tongue. The deep tendon reflexes are lost early in the disease. Muscle biopsy reveals characteristic groups of uniformly atrophic fibres alongside others which are normal.

Congenital muscular dystrophy is rare; as a rule muscular weakness and hypotonia are comparatively slight in infancy and are confined to the proximal limb muscles. Weakness tends to progress slowly as the child develops, but occasionally deterioration is more rapid. Muscle biopsy shows an excess of endomysial collagen and fat, variation in muscle-fibre size, fragmentation and phagocytosis of some muscle-fibres, and even areas of inflammation and fibre regeneration. Patients with the "*central core disease*", which hitherto has been described in only one family, also have muscular weakness and hypotonia, predominantly of proximal limb muscles, from birth. As the child grows the weakness remains unchanged, and there is no apparent progression throughout life. All the deep tendon reflexes in these cases are generally present. Muscle biopsy shows a characteristic abnormality: the fibres are generally larger than normal and contain, in transverse section, a central core of closely packed myofibrils which stain blue, instead of the normal purple, with Gomori's trichrome stain.

Finally, patients with "*benign congenital hypotonia*" also have weakness and hypotonia of proximal limb muscles from birth, but never as severely as in Werdnig-Hoffmann disease, despite the fact that the respiratory muscles are sometimes involved; the tendon reflexes are usually retained, though they may be depressed. Although affected children are late in reaching the normal physical milestones and may not walk until the latter part of the second year or the third year of life, they improve steadily and eventually recover completely. Muscle biopsy reveals either completely normal muscle or a uniform reduction in diameter of the muscle fibres.

As GREENFIELD et al. point out, infantile hypotonia may also be symptomatic of cerebral, skeletal, and metabolic disorders—a feature to which WALTON [9] has also drawn attention—but in these infants muscle biopsy will show no abnormality. They consider briefly the syndrome of widespread muscular atrophy and contractures which has been entitled arthrogryphosis multiplex congenita, but insist that this cannot be regarded as a distinctive disease since microscopic examination may indicate a myopathic lesion in some cases but a neuropathic lesion in others.

This work, although an important step forward, still leaves many questions unanswered. It is true that the muscle-biopsy findings in Werdnig-Hoffmann disease are usually unequivocal; but the existence of a genuine congenital muscular dystrophy remains in doubt, and the syndrome of benign congenital hypotonia has yet to be precisely defined. In WALTON'S [10] series of cases which were regarded as examples of benign congenital hypotonia, half the patients recovered completely; while half, though improving up to a point, had smallness and weakness of some muscles throughout life, thus resembling clinically (though not pathologically) the patients with "central core disease". GREENFIELD et al. suggest that those of WALTON'S cases which recovered incompletely should properly be regarded as examples of muscular dystrophy, even though the weakness was not progressive and muscle-biopsy specimens in several showed no abnor-

1. Greenfield, J. G., Cornman, T., Shy, G. M. *Brain*, 1958, **81**, 461.
2. Werdnig, G. *Arch. Psychiat. Nervenkr.* 1891, **22**, 437.
3. Hoffmann, J. *ibid.* 1892, **22**, 644.
4. Batten, F. E. *Brain*, 1903, **26**, 147.
5. Turner, J. W. A. *ibid.* 1949, **72**, 25.
6. Shy, G. M., Magee, K. R. *ibid.* 1956, **79**, 610.
7. Oppenheim, H. *Mschr. Psychiat. Neurol.* 1900, **8**, 232.
8. Walton, J. N. *Lancet*, 1956, **i**, 1023.
9. Walton, J. N. *Proc. R. Soc. Med.* 1956, **49**, 107.
10. Walton, J. N. *J. Neurol. Psychiat.* 1957, **20**, 144.

mality. Furthermore, there is no place in GREENFIELD's classification for the condition which KRABBE [11] has entitled " congenital universal muscular hypoplasia ", and which is clinically similar to WALTON's " benign congenital hypotonia with incomplete recovery " and to TURNER's [5] " benign congenital myopathy ". One serious difficulty is that the pathological responses of muscle, observed by conventional histological techniques, are extremely limited; and similar appearances may result from several diseases of different ætiology. Perhaps newer techniques, including histochemistry and electron microscopy, will throw additional light on these fascinating but perplexing problems. For the present, however, the physician who classifies his cases of infantile hypotonia according to the findings outlined in the careful study by the Bethesda workers will make relatively few mistakes in forecasting the outcome of the illness.

A " Chest Service "

IN 1956, discussing the proposal that a " comprehensive chest service " should be evolved from the present system of chest clinics in this country, we remarked that " it is hard to believe that diseases of the respiratory system, other than tuberculosis, differ so much in social significance that they need a service that cannot be provided by the general hospital." [12] A year later we suggested that " it would seem better to graft developments in chest medicine on to the local general medical structure, rather than on to the more rigid structure of the tuberculosis service ".[13] The Joint Tuberculosis Council has now published a report on the subject.[14] The Council recommends that " the integration with general medicine which has already begun should be continued ". Future consultant appointments to chest clinics and chest outpatient departments should include membership of the medical staff of a major general hospital, with charge of beds; and further efforts should be made to bring chest clinics " within the curtilage of general hospitals ". Tuberculosis " must no longer be dealt with by a body of physicians isolated from general medicine ". There must be a department of chest medicine in, or attached to, each teaching hospital. The staffing structure of the " chest service requires urgent revision to bring it into line with the staffing structure of general medicine ".

The proposals in this carefully compiled report are considerably different from the ill-defined concept of a " comprehensive chest service " that we previously criticised. We agree that efforts should be made to establish chest medicine as a specialty within the existing general hospital structure (as, no doubt, it already is in some areas); and the Council's recommendations seem on the whole to represent a reasonable way of bringing this about. But the concept of consultants in diseases of the chest being on the staffs of general hospitals is quite different from the idea that the existing chest clinics should be developed into " a service for diseases of the chest ". Chest clinics differ in one important respect from outpatient departments: they are designed to deal with an infectious disease that can be prevented. As the report states, special techniques have been built up for this purpose, including family care, lengthy follow-up, cooperation with public-health departments, and sociomedical and rehabilitation services. The report also says that these services are available in general medical departments, though here they do not suffice for the care of tuberculous patients. But, as far as we know, it has not been suggested that general medical departments should look after tuberculous patients. The crux of the problem, however, is the diagnosis and care of patients with non-tuberculous respiratory diseases. Can this work be done efficiently in hospital outpatient and inpatient departments, or does it require chest clinics, with their special techniques developed to deal with tuberculosis? According to the report, the number of new patients not having tuberculosis seen at chest clinics in the North East Metropolitan hospital region in 1957 was 54,716—an increase of 24% on the number seen in 1953. At eighteen clinics in various regions during one winter month in 1958, 22% of the 3059 new patients had respiratory tuberculosis, 3% had neoplasms, 5% had cardiovascular disease, 27% chronic and 30% acute respiratory disease, and 13% other unspecified conditions. Clearly the proportion of new patients with non-tuberculous disorders seen at chest clinics is increasing, and much of the diagnostic work is concerned with non-tuberculous disease; but the majority of patients with these conditions are probably sent to the clinics for a chest X-ray to exclude tuberculosis and cancer, rather than to obtain a consultant's advice on the treatment of chronic bronchitis or acute respiratory infection. This diagnostic work could, we believe, be done in hospital outpatient and inpatient departments, adequately staffed and under the control of consultants with special training in respiratory diseases: the special structure of a chest clinic is not required. No facts are available on the volume and type of treatment (including the help given by health visitors and tuberculosis care organisers) given to patients without tuberculosis at the chest clinics. What proportion, for instance, of the 27% with chronic non-tuberculous respiratory disease require, or obtain, help that could not be given by general practitioners and suitably staffed hospital outpatient and almoners' departments? It seems likely that most of the 30% with acute respiratory disease required no hospital treatment at all. How many of the 5% with cardiovascular disorders were referred to cardiological or general medical outpatient departments? Only 3% of the patients in the sample were found to have neoplasms. Possibly a quarter of these received surgical treatment, and others would probably be sent to radiotherapy departments. It is, indeed, difficult to see what part of the treatment of non-tuberculous respiratory illness could not be carried out in chest departments of general hospitals or, in many cases, in general medical departments. Is it seriously claimed, for instance, that the treatment of pneumonia or chronic bronchitis requires a unique set

11. Krabbe, K. H. *Nord. Med.* 1947, **35**, 1756; *Acta psychiat., Kbh.* 1958, **33**, 94.
12. *Lancet*, 1956, i, 272.
13. *ibid.* 1957, ii, 478.
14. Joint Tuberculosis Council: a Report on the Future Service for Tuberculosis and Diseases of the Chest. 1958. 1*s.* 6*d.*

of skills and ancillary services not possessed or unobtainable by competent general physicians?

Although the care of patients with lung cancer seems to be a very small part of the work of chest clinics or departments, there is just a little evidence that it might profitably be extended. At the Brompton and Royal Marsden Hospitals the social needs of patients with incurable lung cancer have been surveyed.[15] With the consent of the general practitioners, about half the 155 patients studied were visited in their homes by one of the hospital almoners. Most of the general practitioners welcomed the idea of a hospital almoner visiting their patients, as this preserved contact with the hospital and the consultant after the patient had become too ill to attend the outpatient department. The patients' families also appreciated the continued contact with, and interest of, the hospital; and the first-hand information about the family and the home sometimes helped the hospital consultant in advising on terminal care and readmission to hospital. Adequate care at home was possible for nearly half this group of dying patients. Hospitals and consultants can do little for a large proportion of the patients with lung cancer, and it falls to the general practitioners to alleviate the distress of the final stages of the illness. Possibly more could be done to help them by the hospital chest departments and chest clinics, along the lines suggested by this interesting inquiry.

Much of the work of chest clinics is concerned with preventing the spread of tuberculosis. Can the techniques for this be used to prevent chronic bronchitis, cancer, or heart-disease? Even if they could, it seems unlikely that tuberculosis is at present so effectively prevented in this country that the resources of chest clinics for preventing tuberculosis could wisely be withdrawn from this task. The dangers of some present trends seem to have been clearly recognised by the former secretary of the British Tuberculosis Association[16]: "So many chest physicians . . . are almost ashamed that they handle cases of pulmonary tuberculosis, and seek to emphasize the wide range of other diseases in which they are masters. What a tragedy of perverted thinking! . . . let them beware lest in trying to increase their importance they succeed only in diluting their special ability." Few would deny that chest medicine is a legitimate special branch; that physicians well trained both in general medicine and this specialty have an important role in the hospital services of the country; that the chest physician's wide outlook on the patient and his environment could profitably be employed in dealing with diseases other than tuberculosis and by other physicians; and that it would be economical, as tuberculosis declines, to use well-equipped and well-staffed chest clinics for additional purposes. But it still seems to us wiser to absorb them slowly into the general hospital system rather than to try to develop a "chest service" distinct from, although integrated with, the hospital service. Is a "chest service" really necessary?

15. Bailey, M. *Almoner*, 1959, **11**, 379.
16. Clarke, O. See *Tubercle, Lond.* 1958, **39**, 329.

Annotations

REFORMING THE PRISONS

THE war-time increase in crime, though regrettable, was not unexpected. But ten years of admittedly uneasy peace has brought no recession, and, though the rate of increase has slackened, its continuance has rightly disturbed the community. We are beginning to realise, however tardily, that things are not going to right themselves and that ignorance, inaction, and laisser-faire are not the most effective principles on which to base our treatment of offenders. The white-paper summarised on p. 316 points out that crime changes with the pattern and outlook of society and that penal methods must be adapted to fit it. In a society which is changing as rapidly as ours the need is especially great. The problems which face us today are increases in crimes of violence and sexual offences, a persistent growth of dishonesty, and a startling increase in convictions among young men.

In society itself there has been growing awareness of our lack of information about the roots of crime, the personality of the offender, and the comparative efficacy of different forms of penal treatment. The more varied our methods of treating the offender become, the more important are accurate diagnosis and proper facilities for appropriate treatment. It is little use to recommend a borstal institution for a lad if he has to spend 12 weeks in a local prison before a vacancy can be found for him. The white-paper reviews the tentative beginning of a research programme which is welcome but overdue. Likewise, its programme for buildings demonstrates the difficulty—in prisons as in hospitals—of overtaking years of neglect. Even if the paper plans were already translated into bricks and mortar, or concrete and steel, there would still be 1500 men sleeping 3 in a cramped cell.

Society's responsibility for the offender cannot end at the prison gates. Especially the long-term prisoner needs help and encouragement if he is to re-enter the community successfully. The white-paper describes some of the helpful procedures, such as pre-release quarters and hostels outside the prison, which are being introduced. But much remains to be done, and in a Fabian Society pamphlet[1] Dr. Howard Jones calls for a centrally co-ordinated aftercare service which may be compulsory and which is fully integrated with the management of the case while in prison. This would ensure continuity of treatment and not merely the distribution of small sums of money and well-meaning platitudes to a few "deserving" cases. The untrained voluntary worker may have a place in such a scheme, but Jones rightly insists on skilled supervision. Parallel with this, he wishes to see more hostels for homeless ex-prisoners.

In introducing the white-paper in the House of Commons Mr. Butler announced that he was setting up a committee to study the late Margery Fry's proposal that the community, because it has failed to detect the victim of a crime, should assume responsibility for the failure and pay compensation. With this concept is linked the concepts of personal reparation, discussed in the white-paper, whereby a prisoner should pay damages to the fellow citizen who has been injured by his misdeed. This would of course mean that the prisoner would have to be

1. Prison Reform Now. By HOWARD JONES, lecturer in social studies, University of Leicester. Fabian Research Series no. 203. Pp. 31. 2*s*. 6*d*.

paid a reasonable wage (instead of the present 2*s.* 8*d.* per week). Though there would be obvious difficulties in introducing this system, there would also be clear advantages. It could be a means of re-educating the prisoner's sense of responsibility and restoring his self-respect; it could bridge his return to normal life; and it could (as the white-paper points out) help the public to regard prisoners as "members of the working community, temporarily segregated, and not economic outcasts".

HÆMAGGLUTINATION IN VIRAL HEPATITIS

SINCE the original observation by Hirst [1] that influenza virus can cause agglutination of avian red blood-cells, the phenomenon has been widely studied; and it is now recognised as a property shared by many viruses pathogenic to man and animals. Moreover, the susceptibility to agglutination is by no means confined to avian red cells. Several investigators have found a similar activity in the serum of patients with infective hepatitis; and in 1957 Rubin et al.[2] claimed that this hæmagglutination was due to a specific effect of the hepatitis virus. Havers,[3] however, in a limited study, questions this interpretation.

Havers investigated the hæmagglutinating activity of the serum from 105 patients with infective hepatitis, using as the test substrate red blood-cells from day-old chicks. As a control the sera from 56 healthy medical students, 49 patients with chronic liver disease, 58 with miscellaneous diseases, and 23 with obstructive jaundice were similarly tested. With the exception of the patients with obstructive jaundice, positive reactors were found in all these groups but most consistently in the patients with acute infective hepatitis. Agglutination titres exceeding 1 : 80 were found in 38 of the 54 acute-hepatitis sera tested after less than twelve months' storage at dry-ice temperature, but only 6 positive reactors were found in the group with chronic liver disease and 10 in the miscellaneous group.

The failure to obtain agglutination with the serum from any of the 23 cases of obstructive jaundice is itself an observation of great interest. 9 of these were cases of so-called cholestatic hepatitis, some instances of which are almost certainly due to virus hepatitis.[4] Failure of these sera to cause agglutination is probably due to the presence of an inhibitor, which was in fact demonstrated in the sera of convalescents from hepatitis when the agglutinator was first absorbed by chick red blood-cells.

In view of the many different viruses capable of causing hæmagglutination, the positive reactions obtained with the control sera do not entirely disprove the contention that the reaction with hepatitis serum is due to the specific action of the hepatitis virus. But Havers has shown that the hæmagglutinating activity of these sera is virtually destroyed by heating for two to four hours at 60°C—which is quite at variance with the remarkable thermostability of the virus as regards its infectivity. Furthermore, he has shown that on electrophoresis in starch the hæmagglutinating substance travels with the γ-globulins. Accordingly Havers concludes, with justification, that hæmagglutination by the serum of patients in the acute phase of infective hepatitis is the result of some physico-chemical alteration of the serum-proteins (a consequence presumably of the hepatic damage) and is not a specific effect of the virus itself on the red-cell surface.

1. Hirst, G. K. *Science*, 1941, **94**, 22.
2. Rubin, B. A., Kemp, H. A., Bennett, H. D. *ibid.* 1957, **126**, 1117.
3. Havers, V. P., Jr. *New Engl. J. Med.* 1958, **259**, 1202.
4. Watson, C. J., Haffbauer, F. W. *Ann. intern. Med.* 1946, **25**, 195.

SYDENHAM'S CHOREA

St. Vitus' dance is an ill-understood and often misunderstood condition. There must have been many children who were punished for dropping crockery, lagging behind with their school work, or even making faces at the teacher, before it was recognised that they had chorea. But merely to recognise the disease does not tell us much about it. Not many accept the idea [1] that "lone" chorea may be non-rheumatic. Patients with lone chorea may be found to have developed cardiac lesions when examined later; conversely Lessof [2] described patients in whom mild rheumatic fever was followed by a chorea which outlasted all other signs of rheumatic activity; so it seems likely that in most cases of lone chorea other signs of rheumatism were not observed rather than not present.

Chorea is exceptional among rheumatic manifestations, in that it may be accompanied by no clinical evidence of inflammation. Severe chorea can exist without arthritis, active carditis, or subcutaneous nodules, and without fever, leucocytosis, increased erythrocyte-sedimentation rate, or evidence of other "acute-phase" reactions such as C-reactive protein. In a controlled study Dixon and Bywaters [3] showed that chorea might appear, persist, and even deteriorate despite corticotrophin therapy in doses adequate to damp down most inflammatory lesions. On the other hand in many patients chorea appears as part of their acute rheumatism and improves when the other signs improve or are brought under control by therapy. Lessof believes that chorea may develop in two circumstances—either as a result of active rheumatic lesions or owing to residual brain damage. He maintains that the distinction between active and residual chorea is valid, "just as active rheumatic carditis may be distinguished from established rheumatic heart disease". The concept of residual chorea helps to explain why this disease has no fixed duration, why the disordered movement may recur when the child is upset or nervous, and why antirheumatic therapy is disappointing if there are no other signs of rheumatic activity. But this concept gains no convincing support from studies of the brains of children who have died with chorea. Chorea itself is not fatal, and death results from an accompanying carditis and heart-failure, or possibly from the now very rare rheumatic hyperpyrexia[4]; and it is difficult to attribute any brain lesions to the chorea rather than to the hyperpyrexia or to the venous congestion or anoxia. Bruetsch [5] and before him Winkelman and Eckel [6] showed that the brain does not escape similar damage in children who die of acute rheumatism without chorea. Nevertheless the occurrence of hemichorea strongly suggests that there is a circumscribed morbid anatomical change.

These considerations have some bearing on the treatment of chorea. Sydenham [7] maintained that he cured "no less than five, by bleeding and purging at intervals"; but he practised before the era of the controlled thera-

1. Kagan, B. M., Rosner, D., Rosenblum, P. *Amer. J. Dis. Child.* 1949, **78**, 306.
2. Lessof, M. *Guy's Hosp. Rep.* 1958, **107**, 185.
3. Dixon, A. St. J., Bywaters, E. G. L. *Arch. Dis. Child.* 1952, **27**, 161.
4. Cruikshank, E. K. *Lancet*, 1951, i, 1052.
5. Bruetsch, W. L. *Amer. J. Psychiat.* 1940, **97**, 276.
6. Winkelman, N. W., Eckel, J. L. *Arch. Neurol. Psychiat.* 1937, **28**, 844.
7. Sydenham, T. Schedula monitoria de novæ febris, ingressu. London, 1686. 11th edition (translated by J. Pechey), p. 417. London, 1740.

peutic trial gave us a little more insight. No remedy has been shown to shorten the disease. Lessof observed that 38 of 206 affected children were still choreic six months after the onset, and of 160 patients recalled for follow-up examination 46% still showed occasional choreic movements at an average of eleven months after the apparent end of the attack. Although choreic children are unwell and require a protected environment, long-continued bed rest with sedation may be unnecessary or even harmful if it interferes with the natural functional readaptation of the brain. Lessof adopts the view of Still,[8] who favoured active re-education in coordinated muscle movements for cases of residual chorea. It would be interesting to compare patients treated by bed rest and sedation with those treated by postural and kinetic re-education. The way in which the child's cerebral function is restored after anatomical damage is not well understood; but that such recovery may take place has been shown by Eirene Collis and her associates [9] in the treatment of much more severe disorders of movement, such as athetosis and rigidity.

STAPHYLOCOCCAL EPIDEMIOLOGY

MUCH has been written of late about the prevention of staphylococcal infection in hospitals.[10] Of equal practical importance is new information about the epidemiology of staphylococcal disease, for it is on an understanding of epidemiology that prophylaxis depends. One aspect of particular interest is the worldwide spread of phage-type 80/81, and Dr. Phyllis Rountree, who in 1953 first isolated staphylococci of this new phage-type, has now, with M. A. Beard,[11] given a full account of the organism and of its progress in Australia in the years since its discovery.

Another typing phage, discovered in Canada and given the number 81, is very similar to Rountree's phage 80 and lyses almost all staphylococci lysed by phage 80. A few rare staphylococci react only with one or the other, but the common epidemic type is lysed by both phages and is properly called type 80/81. Thus reports from Canada and the United States referring to type 81 describe the same organism as that termed type 80 in British accounts. Infections caused by type 80/81 were first noted in 1953 in hospitals in Australia and Canada, and since then have been increasingly reported from many parts of the world including Britain, Holland, eastern Europe, the United States, New Zealand, and Uganda. In Australia the strain has spread widely. In the years 1954–57 it caused 70 of the 86 major epidemics of staphylococcal sepsis among infants in maternity units, and it often spread to the mothers and caused breast abscesses; it caused much of the wound infection in surgical wards; and in the community at large it was the commonest type isolated from cases of recurrent furunculosis. This Australian experience emphasises that type 80/81 can cause epidemics in many situations other than hospital nurseries for the newborn, where most of the first reported outbreaks took place. It may infect patients of any age. Last year, for example, in a hospital in the United States 3 out of 6 bacteriologically proven cases of staphylococcal parotitis in elderly medical patients were caused by this staphylococcus.[12] The increase in infections by type 80/81 in Britain has been described by Dr. R. E. O. Williams,[13] director of the British staphylococcus reference laboratory, in an informative analysis of epidemic staphylococci in this country in the years 1954–57. Of the epidemics investigated, 16% were caused by type 80/81 in 1954 and 42% in 1957. He points out, however, that, although 80/81 has become the commonest epidemic strain in this country, types 52A/79, 71, and 7/47/53/54/75 in maternity units, and 75/77 and 47/53/75/77 in surgical units, are also dangerous epidemic strains.

Why has type 80/81 become virtually a pandemic strain? We do not know; but Rountree and Beard suggest that it has two properties—high infectivity and resistance to antibiotics—which together may be mainly responsible. It is clearly highly communicable and often produces unusually severe lesions. Resistance to penicillin is almost universal, and resistance to several antibiotics is common in type 80/81 staphylococci isolated in epidemics. Only among phage-group III staphylococci are so many resistant strains found, and group-III strains do not seem to equal type 80/81 in infectivity. Carriage by healthy people would promote its spread, and Williams has noted that in hospital epidemics due to type 80/81 or other types belonging to phage-group I there are considerably more carriers of the epidemic type among the staff than in outbreaks caused by other types. Other workers,[14] investigating nasal carriage of staphylococci by nurses, observed that when type 80/81 had been found on one occasion in the nose it usually remained for a long period as the carried strain; whereas other hospital staphylococci, although picked up frequently, more often remained in the nose for only a short time.

As regards carriage of hospital staphylococci in general, Goslings and Büchli [15] report from Holland some interesting changes in nasal carriage in patients in hospital and after their return home. During the first two weeks in hospital the proportion of carriers, particularly of resistant strains, steadily increased, but thereafter it remained almost constant. The carriage-rate of penicillin-resistant staphylococci increased in the first two weeks from 3 to 40%. Antibiotic therapy influenced nasal carriage. Patients who received antibiotics acquired resistant staphylococci more commonly than those who did not—a finding also reported by other workers [16] for staphylococci carried in the bowel. After their return home patients who carried penicillin-resistant staphylococci on leaving hospital gradually lost them, but not until more than six months later did the carriage-rate of these strains fall to that for the general community. Not only patients but also some members of their families acquired hospital staphylococci, either through visiting the hospital or from the patient on his return home. Williams [13] believes that the dangerous carrier generally harbours a " dangerous " staphylococcus —one capable of epidemic spread. The work of Goslings and Büchli shows that such dangerous strains, which are common in hospitals, may be readily disseminated by those who have had contact with hospitals, thus lengthening the chain of epidemic spread. Sometimes it is advisable to treat dangerous carriers. Williams [17] considers that routine treatment of carriers of epidemic strains is probably indicated in maternity units, and, in the case of type-80/81 carriers, also in surgical units.

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Special Articles

THE SHORTAGE OF MIDWIVES AND THE FUTURE MATERNITY HOSPITAL

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OF all the jobs undertaken by the medical profession midwifery is the most rewarding. Its aim is normality, and if normality is achieved there is a glow of satisfaction in all those who have assisted the woman in her supreme fulfilment. A great deal of surgery is destructive; but even that which is constructive, though it may give great joy and relief to patient and operator, is but a caricature of normality and a compromise with pathology. The physician has his triumphs and talks of his diabetics and pernicious-anæmia patients as "restored to normal health". Are they? Medical administrators and public health officials all have their self-esteem promoted by seeing the effect of their works. None of them, however, quite reaches the sense of artistic satisfaction that comes of guiding, fostering, and befriending a woman to the creation of a new human being—or indeed the frustration and disappointment when normality is not vouchsafed. The perfect pregnancy and confinement is one of which it could be said in retrospect that the doctor and nurse were unnecessary—at least on superficial thinking.

Why is it then that there is a chronic shortage of midwives? In Britain we train nearly three thousand midwives every year, but within 3 years three-quarters of them have ceased to practise midwifery. Young women come forward for training with a considerable sense of vocation—that is to say they are emotionally stirred at the prospect of aiding in a wonderful creative act. Their own maternal impulses make them want to work in a maternity hospital where they will be surrounded by triumphant happy mothers. Though the young woman coming forward for training may only be able to express herself by "I love babies", there is a wealth of profound healthy emotion behind this sentence. Why then do not nurses fight to become midwives? Why do so many of them give up after taking the part I of the Central Midwives' Board examination? Why do so many who have taken part II give up midwifery and look for other jobs? One expects to lose those who are taking a midwifery training simply as part of their qualification for higher posts in the nursing world, and one expects to lose many of those who marry; but why do so many of the others default? Is there something wrong in the methods of training or employment of these nurses that has soured the enthusiastic relish with which they came to the job? Do they ask for bread, and we give them a stone?

The newspapers, medical administrators, politicians, and the Royal College of Midwives would probably all say that it is a matter of hours of work, off-duty, conditions, and especially pay—but they would be wrong. All these things should be regulated as perfectly as possible; but it is quite amusing to watch the reactions when each improvement is followed by a greater and greater shortage of midwives, so that it becomes more and more difficult to maintain status and conditions for those who do continue to practise. One hears of maternity hospitals being wholly or partially closed down because midwives will not stay on the staff or pupils apply for training.

It is my contention that this evidence of unrest is largely due to the frustration of the sense of satisfaction that should be the reward of the enthusiasm shown by the novitiate. Hospitals are designed and run so as to make the most economical use of the woman-power available. The more "efficient" the hospital the more it resembles the modern shirt factory, where one girl sews cuffs, another puts in sleeves, another makes buttonholes, and another sews on buttons. *None of them feels she has made a shirt.* So in a big maternity hospital one is proudly shown the antenatal section, the labour room, the operating-theatre, the lying-in wards, and the "suspect" ward. But think of the pupil coming to train there, or the staff-nurse working there. Mrs. X may be weeks or months in the antenatal ward and become a friend, at home with her nurses. The moment something exciting happens and Mrs. X goes into labour, she is whipped off to the labour room to meet another lot of nurses; and so soon as the child is born off goes Mrs. X to yet another lot. What joy there is if she meets a nurse who has changed duties, or finds in the next bed a patient who was her neighbour when she lay waiting. The nurses in each of these departments are frustrated and thwarted. Those in the antenatal ward feel that after all the care and attention they have given to Mrs. X it is a poor recompense that some other nurse should attend at the delivery, and those in the labour ward would get great satisfaction if they could see mother and baby flourish and progress after the skill they have expended.

Even the supreme moment of delivery may be made into a mockery for the pupil. It is not uncommon for a pupil who is working in any of the wards to be suddenly summoned to the labour couch to "get one of her cases in". She arrives, and is told by a sister to scrub her hands and don sterile gear. She sees a perineum of whose owner she knows nothing. She ties the cord when the baby is born, and she stands by until the placenta is delivered. After routine inspection, baby and placenta are whisked out of her ken. She tidies up the mess, and goes back to her ward with every feeling that this is a thrilling achievement outraged. If she is working in a lying-in ward she may hope that the mother and baby will come to her own ward, but otherwise she can only pay daily calls to fill in the puerperal details necessary for her case-records. Even in her own ward the department system will work. She may have to do a round of temperatures, or swabbings or bedpans while another nurse does a different sequence. If time-and-motion experts were called in further economies in effort might be made; but the frustration and anticlimax would break the spirit of all but the most devoted young woman.

There *are* satisfied midwives and they can be found mostly in country districts and small hospitals. One hears such expressions as "One of my mothers . . ."; "I had a patient . . ."; "Her husband is . . ."; "She did it last time". These midwives talk of "their" mothers, "their" babies, even of "their" husbands, and they are proud of their achievement in looking after the woman antenatally, during delivery, and afterwards. They do all the nursing duties for the patient from delivering the baby to taking the temperature. They are not too senior to deal with bedpans, nor too junior to be regarded as anything but a friend and a highly skilled colleague by the doctor.

Is there no means of giving to nurses in big hospitals the same sense of satisfaction in their job that is enjoyed

by the district nurse? Can we break through the departmental system in these hospitals so that the patient ceases to be a case, and the nurse ceases to be a factory hand? Is economy of woman-power to be met by ever-increasing subdivision of work, so that in the end each of the workers has no feeling that she has accomplished an artistic whole?

It is my contention that with the maternity hospitals as they are, it will not be possible to produce the right atmosphere. The very buildings themselves will not permit sufficient break-up of the departments. Many enlightened matrons have tried to allocate certain patients to certain of their pupils or staff, but have found it impossible to organise anything but a travesty of the proper sequence of attention. Single rooms are not the solution unless a fantastic level of staffing is maintained. Many patients do not enjoy the loneliness of a single room, and dislike the frequent entry of nurses who are strangers to them. If we could build a hospital that combined the advantages of the small country maternity home with those of the large hospital, both nurses and patients would benefit.

Architects must turn this conception into bricks and mortar, but to my mind the fundamental design should be in the form of a starfish. The central body would contain those services, medical and administrative, that need not be duplicated, such as offices, kitchens, laboratories, classrooms, and operating-theatres. Each of the starfish's rays would be a self-contained small hospital with not more than fifteen beds. The beds might be arranged in 2 five-bed rooms and 5 single rooms, or any other convenient combination. Each group would have its own labour room, ward kitchen, nurses' room, doctors' room, and nursery. It would be essential for the patients in a group to be of mixed obstetric types. Some patients might be antenatal, some lying-in, and some "suspect". Isolation of suspects in a separate ward, as usually practised nowadays, is a mere ostrich-like pretence, for traffic and interchange of medical and nursing staff goes on freely. So far as possible a patient would come into a group and would not be moved out of it. After delivery she would return to what she regards as her own bed. It would be necessary to keep the number of beds in each group small—small enough for each patient to get to know all her nurses, and for every nurse to know all her patients.

Although difficult, it might even be possible to arrange for outpatient and antenatal care to be done by the doctor and nurses of the group that will eventually look after the patient in hospital—instead of the "sheep herding" that now passes for care.

To do a round of bedpans in a big ward is a drudgery for any nurse; but to give a bedpan to Mrs. X whom the nurse delivered 2 or 3 days before would be a pleasure enlivened by chats about the baby over whose welfare they are both concerned. When the mother is discharged from hospital, she feels she is parting from a friend; and the nurse feels pride at having seen her patient and baby through their early trials.

It is my belief that if the principle of giving a nurse the satisfaction of doing a whole job were promoted there would be midwives clamouring to work in the hospitals.

Departmentalism must go. In a job so vital to the emotional development of the patient, indeed of her whole family, we must get rid of the mechanical, impersonal methods that obtain in most big hospitals. We must strive to realise the ideals of individual craftsmanship by a small team that obtain in the best private practice.

CLEAN BLANKETS
NEW BOILABLE BEDCOVER

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To a surgeon wound infection is no new problem, but with advances in treatment it has begun to stand out in greater relief. With the control of streptococcal infections by antibiotics, the "hospital" staphylococcus has threatened to hold up advances in surgery—thus inviting conquest.

The suspicion has gradually arisen that patients admitted to hospital acquire new pathogenic organisms on their skin which the first cut of the surgeon's knife drives into the body. That blankets are an important reservoir of infection has been held for many years (Howie 1956).

Attempts to eradicate infective organisms in blankets by the 'Lissapol'-'Cirrosol' technique (Blowers and Wallace 1955) were hopeful. Bacterial counts by the sweep-plate method showed reductions from 246 to 43 after six washings (Frisby 1957). From the latter trial it became obvious that the blankets no longer resembled blankets: the entire ward stock had to be written off after six months, at a cost of £450. It seemed as if sterilisation of woollen blankets presented an insoluble problem because of the nature of the material.

Specification for the Ideal Bed Cover

In attempting to find a blanket substitute it seemed reasonable to define the qualities in the material sought. These fall naturally into two groups: social or housekeeping qualities, and hygienic or surgical requirements:

Social Requirements

The material must provide warmth comparable to the conventional wool blanket.

It must be of about the same weight.

It should be easy to handle, soft, and flexible.

It should not pull out of shape easily nor catch on projections of the bed. A smooth surface would be an advantage.

It should be easy to clean and wash, and be resistant to the usual washing-soaps, detergents, and bleaching agents.

It should be hard-wearing and look "as new" for at least a year or two. It should not shrink or alter in texture.

It should be reasonably cheap initially and cheap to repair.

It should be resistant to moths and other household pests.

It should be easy to store.

Surgical and Hygienic Requirements

It should be capable of being sterilised by boiling. It should be capable of being washed at regular intervals without appreciable deterioration. A set of clean blankets for every patient on admission to hospital should be a minimal requirement. In certain cases, being able to change the blankets as frequently as the sheets on a bed would be an advantage.

The technique for washing the blanket should not be complex, and preferably should not disrupt the normal laundry routine.

It should not actively attract bacteria.

It should be capable of being rendered bacteriocidal for an appreciable time.

It should not produce fluff.

A Substitute for Woollen Blankets

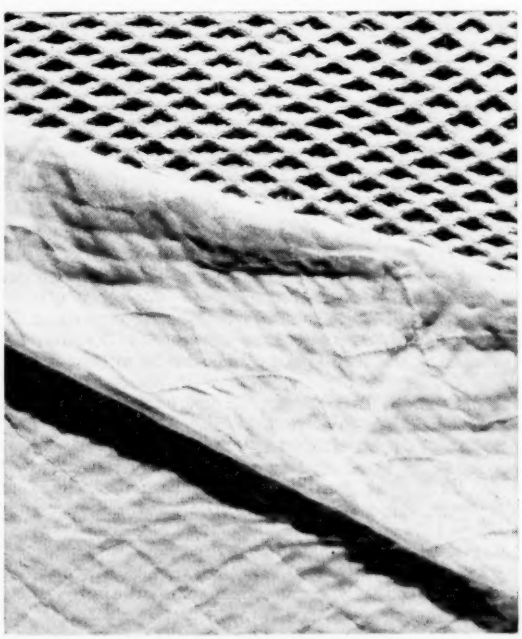
Since it seemed unlikely that the conventional woollen blanket would ever conform to the specification mentioned above, an entirely new approach was needed. Following

COMPARISON OF PROPERTIES OF NEW " BLANKET " WITH THOSE OF CONVENTIONAL WOOL BLANKET

Property	Conventional wool blanket	New " blanket "
Cost related to that of a single-bed sheet	× 3–4	× 2½
Weight (oz.) per square yard	15	22
No. per bed (index of relative warmth)	3	2
Size (in.)	66 × 86	56 × 90
Life (yr.)	About 9 (no washing)	3¾ (that of a sheet) (? 150 washings)
Shrinkage (%) on washing	20% or more	5–6
Fibres	Short; break off easily and create fluff	Long; no fluff

discussions with Mr. W. Trillwood in June, 1955, it was decided to start with one quality—warmth—and examine materials with this property. The successful British Everest expedition had proved once again the value of a string vest under conditions of extreme cold, and Dr. Charles Evans (personal communication) confirmed the warming properties of these vests but pointed out that they were warm under those extreme conditions only when a wind-proof garment was worn over them. Courtaulds Ltd., who had supplied the expedition, kindly sent a bed-size portion of the material for inspection. It had originally been planned to use this cellular material loosely between sheets, but because of the nature of the material it soon became obvious that bed-making was likely to become a most tedious ward duty. Moreover the original material, of viscose acetate, could not be boiled without deterioration.

Another cellular material of viscose staple and cotton was therefore used, and this was quilted between two cotton sheets. The resultant composite bedcover looked much more promising. Owing to certain manufacturing difficulties at the time, these substitute " blankets " were not wide enough to give sufficient tuck-in for the thick mattresses that were used in the wards, but a 2-feet-wide piece of sheeting sewn along each side of the " blanket " easily corrected this minor fault.



The three layers of blanket-pad.

Sufficient blankets were provided to run a trial in a four-bed ward, allowing two blankets per bed which were changed every week. In order to avoid making the trial artificial, the only restriction imposed was that no woollen blankets were to be admitted to the ward. For purely administrative reasons the patients in this trial ward were all male. Another four-bed ward, of female patients using the conventional wool blankets, was used as a control. The full clinical trial with bacteriological control was begun in September, 1957.

Description of Blanket

The blanket pad consists essentially of two 'Fibro'-cotton sheets between which is placed a warp-knitted mesh fabric of fibro-cotton blend yarns. The three layers are then sewn together on a needle machine in the form of a quilt, the diamond stitch having dimensions 2 in. side and 3 in. diagonal. The final product thus contains a large amount of trapped air which prevents loss of heat through its substance.

The blanket pad measures 56 in. × 90 in. and is taped along the four sides. Sheeting along each of two sides allows sufficient material to tuck in, thereby reducing the cost and bulk. Blanket tucked under the mattress provides no useful purpose other than as a point of fixation and on hospital beds is the portion most likely to be torn. Replacement of the sheeting sidepieces is cheap and simple.

The make-up of the three-ply construction is shown in the accompanying figure.

The properties of these blanket pads are compared with those of the conventional wool blanket in the accompanying table.

Results of Trial

During the past thirteen months 96 inpatients admitted for operation have slept in one small surgical ward using the new blankets. All the patients found these blankets comfortable and warm and several patients were even unaware of anything unusual about the bed coverings. One patient asked for three blankets on his bed but later discarded one of them, and two patients found that a single blanket on the bed was sufficient even in winter. One man noted that when he had to go at night to the toilet his bed was not as warm to " welcome him back " as he had expected, but this lack of warmth was not confirmed by other patients to whom the specific question was directed. The average temperature in the ward throughout the year was 65° F.

Following the introduction of the blanket pads there was a noticeable reduction in the amount of dust and fluff on the floor in the ward, which was remarked on by both patients and staff. The nursing staff found bed-making no more irksome than usual; and indeed it seemed easier to discard all the bed coverings instead of the sheets alone, as in other wards using conventional wool blankets, when the sheets were changed on discharge of a patient.

The patients from the trial ward underwent a wide variety of plastic surgical operations, the majority being major surgical procedures. The incidence of wound infection was a little lower than in patients from the other plastic-surgery wards; but the figures are of little

value since the incidence of wound infection in the whole unit, which has varied within wide limits over past years, was at an unusually low level. Smears of suture lines (at the time of removal of sutures) on patients, both in the trial and in the control wards, commonly grew staphylococci even though undoubted primary healing was occurring.

The bacteriological aspects of the trial are fully dealt with elsewhere (Frisby 1959). At the end of one year the original blanket pads are still in use and appear to be little changed in texture. There has been some shrinkage of the quilting stitch, giving the blanket covering-sheet a seersucker surface.

Discussion

The bacterial content of dust has been held to be a likely source of infection in hospitals. Methods are already available for the effective removal of ward dust, but, since much of this presumably comes from short-fibre material used as bed coverings, the new blanket described here was designed to eliminate dust. The production of a blanket which could meet certain requirements of ordinary hygiene was the first stage in the attempt to control serious cross-infection in hospitals. The second stage, consisting in methods of sterilising the blanket and preserving " relative sterility " for a reasonable time, has also been completed (Frisby 1959). The third stage in this investigation—namely, improvements in the design and in the methods of laundering the new blanket—continue with promise.

I am indebted to Courtaulds Ltd. for the supply of trial blankets. 'Fibro ' is the registered trade mark of Courtaulds Ltd. for their viscose rayon staple. The blankets are now being manufactured by Slumberland Ltd., Tyseley, Birmingham, 11.

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Dialogues of Today

SHOULD THE PUBLIC KNOW?

APOLLODORUS: Welcome, Socrates, you have come just at the right moment. Eryximachus is upset because some of the teachers of medicine have been standing up in the market-place telling anyone who cares to listen about health and disease.

ERYXIMACHUS: Not only that, Socrates, but they have been writing books about medicine which anyone can buy and understand, and that is contrary to the regulations of our sacred college.

SOCRATES: Tell me, Eryximachus, why you think they ought not to do this?

ERYXIMACHUS: Because, Socrates, it takes many years' training to understand medicine, and, since the layman has not that training, he will not fully understand what these people tell him, and he will be filled with unreasonable fears about his own health. Indeed I am told that some of those who listen to these lectures drop down in a faint, and injure themselves.

SOCRATES: Do you think, Eryximachus, that knowledge is good in itself or only for some purpose?

ERYXIMACHUS: Some knowledge, Socrates, is good in itself; but that is not the case with medicine, which is for the purpose of healing the sick, and should be restricted to those who have the training to practise the art.

SOCRATES: Is it better to be ill or well, Eryximachus?

ERYXIMACHUS: To be well, Socrates.

SOCRATES: And to prevent sickness or to cure it?

ERYXIMACHUS: To prevent it.

SOCRATES: And is a knowledge of medicine necessary to prevent sickness?

ERYXIMACHUS: Yes, in many instances.

SOCRATES: Then if a layman is to keep himself in health, he must have some knowledge of medicine?

ERYXIMACHUS: I suppose so, Socrates; but only of the kind which his own doctor can teach him.

SOCRATES: Do doctors give their patients such instruction?

ERYXIMACHUS: No, they are too busy curing their diseases.

SOCRATES: And if they had the time, would they all have the requisite skill in teaching, and the means to illustrate their instruction?

ERYXIMACHUS: Most of them would have had no experience of such work.

SOCRATES: So it would seem, would it not, that if laymen are to learn to prevent sickness they must be taught by those who have the skill and the means to teach them? But tell me, Apollodorus, do you think a knowledge of history good?

APOLLODORUS: Yes, Socrates, for without a knowledge of the past we cannot understand the present.

SOCRATES: And of science?

APOLLODORUS: Yes, indeed, for science enters into all aspects of modern life.

SOCRATES: And does not medicine enter into all aspects of modern life? Is not the parent continually having to decide whether to let his children submit to some procedure designed to prevent sickness in future, and is not the employer required to take steps to prevent his workmen from contracting diseases at their work? And is not the citizen called upon to serve on many committees deciding about health and sickness and controlling doctors, and sometimes to decide in the courts whether the act of a criminal is affected by the state of his mind? And is it not in his name that the State proposes to take measures for the treatment of those who are mentally ill, and to prepare for a war which would produce worse diseases than have ever occurred in peace and would inflict them upon all citizens?

APOLLODORUS: All that is true, Socrates.

SOCRATES: And will not the citizen play his part in all these matters better if he knows something about health and disease?

APOLLODORUS: Certainly he will.

SOCRATES: And if the State is responsible for the health of the people, do not all citizens share this responsibility?

APOLLODORUS: Yes, indeed.

SOCRATES: Tell me, Apollodorus, when the State has to decide matters concerning the health of the people or the welfare of medicine, do the doctors express their views?

APOLLODORUS: Certainly, Socrates, very vigorously.

SOCRATES: And does the State pay attention to them?

APOLLODORUS: Sometimes it does, Socrates; but often the doctors' views receive little attention because they are said to be influenced by their own interests.

SOCRATES: Who then decides such matters?

APOLLODORUS: Servants of the Government, Socrates.

SOCRATES: And why do not the lay citizens in the assembly control the servants of the Government in these matters?

APOLLODORUS: Because they do not know enough about health and sickness to do so, Socrates.

SOCRATES: Then it would seem, would it not, Eryximachus, that medicine should no longer be a mystery restricted to a sacred college, but that that State will be most healthy and prosperous whose citizens best understand the nature of health and disease?

ERYXIMACHUS: So it would seem, Socrates.

SOCRATES: And will not the citizens of such a State think more highly of their doctors than those who are entirely ignorant of their work, and lend them their aid against the tyranny of the servants of the Government?

APOLLODORUS: Eryximachus has fainted, Socrates!

Public Health

HEALTH AND SOCIAL CLASS

ADDRESSING a conference of the British Sociological Association on Jan. 24, Dr. J. N. MORRIS, director of the Medical Research Council's Social Medicine Research Unit at the London Hospital, touched on three problems.

CONDITIONS ASSOCIATED WITH POVERTY

As is now well known (Dr. Morris began) infant-mortality rates have been falling in all classes since 1911 when the first of these analyses was made; but so far, according to the Registrar General, there is no evidence of a narrowing of the gap between the social classes:

Class	I	II	III	IV	V	Excess V/I
Neonatal Mortality (1st 4 weeks of life)						
1930–32	21·7	27·2	29·4	31·9	32·5	50%
1949–53	14·0	15·6	18·3	20·0	22·8	63%
Post-neonatal Mortality (Rest of 1st year)						
1930–32	11·0	17·8	28·2	34·9	44·6	305%
1949–53	4·7	6·0	10·4	13·7	18·0	283%
1949–53 as proportion of 1930–32 ..	43%	34%	37%	34%	40%	..

Rates per 1000 live births.

" Social class," in the scheme of the General Register Office, is based on job-skill and status, which in turn are correlated, if only broadly, with education, money income, general standing in the community, and residence. Most of the designing of " social class " was done fifty years ago, but " class " remains a highly effective if crude technique for the analysis of the social economics of our society. Classes I (the upper professional and business families) and V (unskilled labourers) seem to be reducing their infant mortality in fairly equal proportion, although it is probably easier for a fall to occur from high rates than from low, and class V has much higher rates than class I. Classes II, III, and IV are also showing similar reductions. Through war and peace, slump and boom, harsher days and Welfare State, infant-mortality rates have descended along these tramlines.

It is tolerably certain that class differences—they are substantial—in size of family and in the ages at which mothers bear children play unimportant parts in these surprising trends. Two main hypotheses have been advanced in explanation.

One is *culture lag*—that it will take longer for the less educated sections of the population to benefit from the newer knowledge of child-rearing and to take full advantage of services provided and of the advances in medical science. Again, although there has been a substantial rise in the wages of the poorest, and some general levelling of current money incomes and ways of living since 1940, gross differences remain in the " capital " goods of different classes, such as housing amenities if not actual living-space. The healthiness of the mother who may have spent her own childhood in very different circumstances from today has also to be considered in such historical comparisons.

Another explanation emphasises *social mobility*—the rapid turnover and changing composition of social classes. (As Glass and his colleagues have shown, our class structure is anything but rigid and there is considerable mobility up and down the social scale.) The interesting suggestion by Illsley and others is that the healthier move up and the unfit down, so that in a kind of obstetric or pelvic meritocracy social class I is continually being invigorated and producing low death-rates while class V, which anyhow is contracting in size, collects those of each generation who cannot cope—physiologically or socially. But there are consistent inequalities between the infant-mortality rates of particular *occupations*—let alone between *social classes*—that continue over the years—e.g., miners (always high) *v.* textile workers (not so high) *v.* clerks (always low). Such an explanation must needs postulate a tidiness in social and biological rearrangement beyond our own imagining, or, even, our colleagues' computation.

There is very little information on the genetic aspects of the whole problem. Clinical field studies among the families of a variety of occupations and localities are urgently needed.

For example, coalminers now have about the highest earnings of all workers—they are affluent enough—but they also have about the highest infant mortality; which is against so much we believed and hoped in the 1930s. (Perhaps the Coal Board needs a Member for Maternity and Child Welfare—or will the National Union of Mineworkers set an example? There are precedents, if in unexpected places.) Social scientists are strangely reluctant to enter this field which seems an ideal one for " multisciplinary " study. The very few sociological surveys that have been done in coalmining communities, as in Yorkshire, raise issues about family life and parental roles, about values and aspirations, about the extent to which " middle-class " attitudes are and are not spreading, that from the first are directly relevant to studies of infant mortality.

The simple question-raising and elementary social criticism illustrated in these figures of infant mortality are a good example of the value of the analysis by occupation and social class made possible by the General Register Office in an age when the simple and the elementary are no longer fashionable.

Adult Mortality

In adults, among the diseases that show the traditional poverty pattern—i.e., a substantially higher death-rate among the economically under-privileged—recent history is the same. Whether such diseases are declining (e.g., rheumatic heart-disease and pulmonary tuberculosis) or just beginning to decline (e.g., and lagging behind the States, cancer of the stomach) or reportedly increasing somewhat (e.g., bronchitis), class positions are unchanged. In 1949–53 there was as big a gap as before between the death-rates in social class I and social class V, as great an excess in class V. And yet, as Rowntree showed, there had been a transformation in the nature, amount and distribution of poverty since the 1930s. Nor is this picture of biological immobility in a highly fluid society any less sharp if comparison is limited to class III, the skilled and blackcoated, *v.* other workers or is extended to their wives. General investigations, as of " class V ", were badly wanted, and specific ones, as of occupation and gastric cancer—including insights from genetics and from social science as well as from medicine.

The Revolution in Childhood

But in children (Dr. Morris continued) the position is different. Something of a revolution has taken place and we can now speak of a closing of the gap between social classes, of greater equality in health. Thus the death-rate among *children* from rheumatic heart-disease—he used to regard this as the most sensitive of the poverty indicators—has fallen most among the towns and villages of South Wales which formerly had quite frightful rates, and more among the poorer communities generally than in the more prosperous. At the very beginning of childhood, at 1–2 years of age, the gap in mortality between social

class I and social class V is now only a fraction of what it was twenty years ago:

MORTALITY PER 1000 AT 1–2 YEARS

Class	I	II	III	IV	V	Excess V/I
1930–32	4·5	7·3	12·6	15·7	23·0	411%
1950–51	1·9	2·2	2·2	2·4	3·1	63%
1950–51 as proportion of 1930–32	42%	30%	17%	15%	13%	..

Further search among the infant death-rates already quoted has made it possible to locate the start of this improvement in the last three months of the first year of life. The experience then has been quite different from that in the rest of infancy—a nice problem for pædiatricians and immunologists and students of growth:

POSTNEONATAL MORTALITY

Social class	4 wks.–6 mos.		6–9 mos.		9 mos.–1 yr.	
	1930–32	1949–50	1930–32	1949–50	1930–32	1949–50
I ..	7·4	3·3	1·9	0·6	1·7 } 2·8	0·8 } 0·7
II ..	11·2	4·0	3·6	1·0	3·0 }	0·7 }
III ..	16·8	7·4	6·0	1·7	5·3	1·1
IV ..	20·2	10·0	7·8	2·3	6·9	1·4
V ..	25·2	12·5	10·2	2·9	9·2	1·6
Excess V/I	241%	279%	437%	383%	441%	100%

Joint Inquiry, Social Medicine Research Unit and General Register Office.

It is possible further to say that all this change has taken place since 1939.

These exciting signs of another equality, and a new quality, of our society—it may be the first such change in modern history—can be discerned elsewhere. There is little doubt from the data of Douglas and his colleagues that the story is the same in such a disease as chronic otitis media. Very likely it is true also of the important group of lower-respiratory infections. It may be that children are more responsive to the immediate environment than infants and the social and medical advances of recent years have paid off rapidly. Pædiatrics—and orthopædics—and dermatology have already been transformed. Rickets, from being *the* characteristic disease of Victorian England and endemic till the 1930s, is now an uncommon disorder of the metabolic ward. Are we getting to the last lap in serious physical disease of childhood? Will there be a wave of equality back into infancy and on to adult life?

Dr. Morris then turned to two other problems, one in the transition to adult life, the other of middle age. In one, he said, it seems possible to explain some of the social class distribution, in the other to explain some of it away.

CONCENTRATION OF SCHIZOPHRENIA IN SOCIAL CLASS V

First, he dealt with what he called a basic problem in the epidemiology of mental disease, and of public health—the preponderance of schizophrenia among the unskilled young men of social class V. Originating in the ecological work of Faris and Dunham before the war in Chicago, the observation has been something of a storm centre ever since. The latest figures of Brooke were quite specific for England and Wales:

First Admissions for Schizophrenia (per 100,000 men aged 20 and over) in 1949–53 in the five social classes

I	II	III	IV	V
51	57	93	103	229

The concentration in class V is considerably greater when men under 35 only are considered. Is it true? If true, is it due to movement downwards of the mentally ill into unskilled labour and social class V; and/or does the social and familial environment of social class V help to produce a lot, an excess, of schizophrenia?

Two colleagues of Dr. Morris's in the Social Medicine Research Unit are working on this problem.

E. M. Goldberg is approaching it clinically by interviewing the families of a representative series of young men admitted to hospital for schizophrenia, trying to get a picture of the family over three generations, from grandparents to the patient and his sibs.

S. L. Morrison, with the ever-ready help of the General Register Office, has classified a national sample of schizophrenics aged 25–34 by occupation and social class, and then gone back to their birth certificates and classified the patients' *fathers* by *their* occupation and social class at the time of the birth. The answers so far are pretty clear, and in agreement. There is a heavy concentration of patients in class V, but the fathers now (and when the patients were born) are quite ordinarily distributed among the social classes of the population. A downward drop of the patients from the parental status because of their illness seems to be explaining their peculiar social-class distribution. Moreover, there is little evidence in the clinical study that the patients have themselves "drifted" down at all: they seem rather to be non-starters in their parental class after leaving school. This finding is very different from that of Hollingshead and Redlich in New Haven, where the fathers of the patients also were very much what we would call social class V, and a means of cross-checking with the Yale workers having regard, for example, to diagnosis will have to be found.

THE "NEW" DISEASES

The historical trends were highly interesting. The "newest" of all, poliomyelitis, shows a striking excess of mortality (and presumably of incidence) in social classes I and II (farmers!); which is very suggestive in light of the views of Paul, for example, on the *inverse* relationship of paralytic poliomyelitis to the level of sanitation and to the rate of infant mortality. Coronary disease and leukæmia, which showed an excess of mortality in class I in 1930–2, now show a smaller one. Lung cancer and duodenal ulcer, which showed no trend with social class twenty years ago, now give evidence of rising mortality with *descent* in the social scale from class I to class V. How much the spread of diagnostic standards through the population is responsible for such changes it was impossible to estimate.

Social Class and Physical Activity of Work in Coronary Heart-disease

Finally, Dr. Morris considered "coronary thrombosis", the most important of the conditions with a particularly high mortality in class I, though there are technical snags in accepting the actual figures published by the General Register Office. Even before the disease became epidemic, Osler had commented on "the remarkable fact" that angina "is an affection of the better classes" (imagine *The Lancet* allowing anyone today to write of "the better classes"!). The similarity of food intake, including fat consumption, animal and vegetable, processed and natural, among the different sections of the population since 1940 makes it unlikely that nutrition is responsible for the class differences in mortality in 1949–53. The recent national necropsy survey suggests that much of these differences are in fact the product of the connection between coronary heart-disease and physical activity of work. The higher the status, the more light jobs. Light workers of classes I–IV show the same rates of ischæmic myocardial fibrosis in this survey and there is no variation with social class among active workers or in heavy workers. An analysis has now been made of Occupational Mortality data, dealing with deaths actually ascribed to coronary heart-disease, and grading the occupations wherever

possible by the physical activity typically involved. (This kind of analysis would be more difficult in the future because the General Register Office were reducing the number of occupations from 600 to 200 and thus increasing the heterogeneity of many.) The main result was that light workers show similar death-rates at 45–54 years of age, whatever their class, and similar rates in classes I, II and III at 55–64. Mortality among active workers does not vary at all with social class; and among heavy workers there is a strong relationship only at 55–64 years of age:

MORTALITY FROM CORONARY HEART-DISEASE ACCORDING TO OCCUPATION

Social class	Ages 45–54			Ages 55–64		
	Light	Active	Heavy	Light	Active	Heavy
I	176	..	..	568	..	..
II	167	118	..	515	404	..
III	173	137	111	529	444	422
IV	153	121	116	422	380	341
V	175	145	91	424	409	283
All	173	135	102	528	422	399

Rates per 100,000 men, England and Wales, 1949–53.

That is to say, there is no trend with social class apart from physical activity of job at 45–54, and at 55–64 an important one only in heavy workers. (Nor does inclusion of deaths from so-called " myocardial degeneration " make any difference.) The class distribution seems to be mainly dependent on the proportion of light and heavy workers in each class. A reduction of muscular effort in work is one of the striking features of both industrial revolutions and part of the change underlying all the other changes.

THE FUTURE

As the diseases of poverty, ignorance, and malnutrition recede, we confront problems that are manifestly as closely linked to the mode of life—but not in such manifest ways. Moreover, there is no comfort that further social progress—a rising standard of living—will in time mitigate and abolish *our* problems. Here is considerable scope for the expansion of social-medical inquiry, and Dr. Morris appealed to his hearers to help.

Smog

ACCORDING to some observers, the smog in parts of the North-West of England last week was the worst in living memory. The demand for hospital beds increased sharply.

In Salford the foggy period was characterised by a widespread smoky haze with a visibility of never more than 200 yards; the smoke averaged 120 mg. per 100 c.m. and sulphur dioxide 35 parts per 100 million. Late on Jan. 29 the average smoke content was 415 mg. per 100 c.m. After being left overnight the smoke stains were too dense to permit of measurement, but the amount of sulphur dioxide was found to be 109 parts per 100 million—i.e., about six times normal. On the morning of Jan. 30 the smoke and sulphur dioxide levels were 478 mg. per 100 c.m. and 164 parts per 100 million —i.e., about eight times the normal January average.

The demand for hospital beds necessitated putting into operation " emergency " plans whereby hospitals refused certain non-urgent cases. The demand for beds was particularly great in respect of elderly women. Moreover, acute respiratory disorders in patients already occupying beds in acute hospitals resulted in an increase in the number of " blocked " beds.

The public are increasingly conscious of the nuisance of loss occasioned by smog; and, if newspaper columns are an indication, public opinion is now decisively in favour of a speed-up in the implementation of the Clean Air Act, 1956. But, curiously enough, the " black areas " —where fogs are most frequent and where the mortality and morbidity from chest disease is highest—are the areas where there have been fewest applications to the Minister of Housing and Local Government for confirmation of " smoke control " orders.

Smoke Control

Mr. Henry Brooke, Minister of Housing and Local Government, would like to make faster progress in removing the smoke pall from the " black areas " of England and Wales. He has asked councils in these areas to inform him by the end of June how long it will take to deal with their domestic smoke problems, what smoke-control orders will be needed, and their order of priority. He is asking for five-year phased programmes.

In the last two years more than 125 local authorities in England and Wales have decided to use their powers under the Clean Air Act to make smoke-control orders. 33 of these orders are now in operation, and over 190 more have been confirmed by the Minister or are being prepared. Nearly 232,000 buildings and some 39,000 acres of land are, or will be, covered by them.

The Widdicombe File

LII. STILL WAITING

MY DEAR JOE,

I was sorry to hear that you hadn't been appointed to the job at the Elsewhere General Hospital—though for their sake, not for yours. Their hierarchical system may be defensible in theory, but it means that one can be on the staff for thirty years before having full clinical responsibility for one's patients. You'd have been just the man to challenge that idea, but your chances of success would have been slim. Even if you'd won, the victory would have been pyrrhic, and the ulcer you've developed in your seven years as Senior Registrar would have become intolerable.

Allow me to congratulate you on what I hear privately was a narrow escape. Even the best of friendships can't stand the strain of much good advice, but do accept this piece—you really must *see the place* before you apply. I know it means travelling all over the country, and that not many Regional Boards will pay for your expenses on a preliminary survey. So you'll be out of pocket, and the children may have to go without new shoes for another month. All the same, the money will be well spent.

" When am I going to get a job? " you ask. You've had your Fellowship ten years, and a respectable Mastership for three, and your academic record is good. You've been long enough at a good provincial centre to have lost the fine gloss of your London teaching hospital, and to have developed an appetite and considerable ability for hard work. I think you must be 37 or 38, and so long as your present chief is prepared to push hard (some aren't, you know) the outlook should not be too bad.

For one thing, you've been on the market so long that your continued presence is an embarrassment to your seniors. This may be turned to account by appearing at meetings and conferences. If you can read a paper, so much the better. If not, you can tactfully remind various people of your existence.

Of course one can't please everyone. For some time I wrote nothing, because I'd nothing worth writing. My then chief pointed out the great gap this left in an application, so I dutifully scraped out the bottom of the bucket,

and various editors published the stuff. You may not be shortlisted if you haven't published a paper or so; but when you're interviewed, some committee member will almost certainly ask why you wrote *that* paper, or how you found time to produce *this*. They won't have read the papers, and it's always easy to sneer at something one doesn't know.

They'll also ask why you want this particular job. The reply to this is simple. They know it and you know it, and they know that you know that they know it. The answer is in two parts:

1. I have a wife and four children, a mortgage, an overdraft, a peptic ulcer, and a widowed mother, and I don't want to emigrate.

2. I have been saying yes-sir, no-sir, three-bags-full-sir to my seniors for fifteen years, and am fed up with it.

You may have the courage to say this. I didn't. I've long thought that candidates should not appear in person, but be represented by counsel.

Don't be too upset at being rejected. After a while one realises how profound a truth lies in the apparent cynicism of the saying "Blessed is he who expecteth nothing, for he shall not be disappointed". From a long experience I can testify that that is the sovereign safeguard against disappointment.

Your visit to the Board's sumptuous headquarters and the cup of British-Railways-type tea will impress on you the sort of disease service to which you are committing yourself. You'll get the latest news from the grapevine, and may even hear of a promising death vacancy before the obituary is in the press. You'll have excellent opportunities for practising the higher variety of Lifemanship on your fellow candidates. (A play will one day be written about what goes on in the anterooms of Regional Boards.) However wet the day and grey the soup, you can console yourself by thinking that at last Mr. Blank will have to do his own outpatient clinic.

One of his colleagues the other day finished off a conversation on Senior Registrars by saying brightly "Ah yes, but they all get jobs eventually; or they emigrate". *Eventually*. If forty years in the wilderness was good enough for Moses, what are you bleating about? *They emigrate*. As one who nearly did, I wonder if these comfortable gentlemen know the heart-searching, the uncertainty, the ache of torn-up roots, the bitter taste of failure and disillusionment, or the courage in those words.

Your wife, though she does not feature in your application form, is one of your greatest assets. I have the greatest respect for all like her. I married one. They accept us on the strength of some dubious promise, they fulfil all their vows, for better for worse, for richer for poorer, in sickness and in health. They continue to believe in us when we have lost faith in ourselves and in our gods.

Seen from the other side, committees realise that when they appoint a man they also appoint his wife, and I am told that one committee chartered a bus to bring all the candidates and their wives to the hospital.

The selection of an applicant for a permanent post is a grave matter, which may explain if not excuse the devious practices of some Boards. Some candidates put themselves out of the running by the lack of order in their applications. Some are so full of panache and stuffing that they're thrown out, and some so reticent about their achievements that they do themselves no justice. To these I recommend the saying of Artemus Ward "Whoso bloweth not his own horn, that horn will not be blown".

Having selected the applicants from this written record, one must choose one from the short list. The methods in use can be applied singly or in combination:

(1) *The Interview*

There is considerable evidence that one short interview is an extremely unreliable way of choosing a candidate.

(2) *The Ward Round*

Under pretence of showing candidates the department, one conducts a full ward round, pumping them tactfully. Only the most naïve will be taken in by this.

(3) *The Sherry Party*

Provide a few bottles of sherry and mingle the existing consultants with the candidates. This is agonising. The teetotaller will be suspect, and the pint-of-bitter man will be unhappy with Tio Pepe. He may even commit the social crime of preferring a sweet sherry. On such small matters great ones depend. Everyone is ill at ease. One does not even get enough sherry.

Canvassing is prohibited. Anyway, it is not only illegal but unnecessary. Nobody would canvass when there are so many other ways of getting on. To have married the external assessor's daughter a decent time before is an undeniable advantage. One has sometimes felt that the University Representative in fact represented the successful candidate, and should have been asked to declare his interest. A few sheep have been appointed, because they were known to be docile and to have no chance or desire to compete in private practice. Having been at the right medical school seems to help—"You can always tell a —— man, but you can't tell him much".

Conversely, knowledge of how to escape appointment is worth having. One day you may find yourself dangerously near getting the job you don't want, having discovered its drawbacks too late. This nearly happened at Elsewhere, though at the time you didn't know it. In such circumstances, throw away your carefully nurtured conformity. It's just as damaging to say that in your spare time you are a lay preacher as that your two mistresses really leave you no spare time at all.

Appointment committees do have a very hard and thankless task. Out of fifty applicants, probably twenty are well trained, fifteen excellently, and five superbly. Any one of forty could do the job well, and the moans always come from those who aren't appointed.

One imagines, despite all previous experience, that getting a consultant job solves all problems. But, if you look back at any achievement, you will remember that all it did was to raise you a little higher, so that your horizon was farther off. The problems solved are replaced by different and larger ones. The door which will one day open for you won't be only that of the Staff Common Room at St. Somebody's, with its view of the colleagues with and against whom you must work for twenty-seven years, but the entrance to opportunity.

"It is not given to man to command success, but to deserve it". When the door does open, you'll have to think what you mean by success, and in the process will probably discover yourself, and that's what makes all the waiting worth while.

If you didn't live so far away, we could have said all this over a glass of ale and saved you the trouble of reading it. Greetings to Mary and the children.

Your affectionate cousin,

ROBERT STEWER.

In England Now

A Running Commentary by Peripatetic Correspondents

CAN you not hear the hum of the 'Neon' lighting, like the noise of insects hovering over a reedy pond? Can you not hear the pages of the journals being turned thirty or forty yards away—crisp as an old-fashioned five-pound note? Now a student in crepe soles squelches past, followed by a secretary, her high heels tapping like a typewriter. I can only suppose that the practical aspects of library building are so sadly neglected because the powers-that-be have never had to spend long hours there. As a deafened reader, may I respectfully offer a few suggestions?

This parquet flooring, which, with its herringbone design, shines like an old viva suit, is not only noisy but distracting: one is always waiting for somebody to break the neck of his femur. I make a plea for carpets—or even for strips of carpet if the treasurer is likely to quibble. Failing carpets the librarian might keep a supply of raffia sandals for readers.

Cupolas are definitely bad for libraries because they act like the dome of St. Paul's in miniature. We have seen the poor librarian blush seventy feet away when students swapped familiarities.

These smooth, cream, plain, solid walls and the smooth, cream, plain, solid pillars rising to the ceiling doubtless accentuate the simplicity of modern architecture. But, though they reflect light waves (good), they also reflect sound waves (bad). We must turn back the calendar. These surfaces must be covered in heavy damasks or in intricate tapestries depicting the Great Medical Masters. Aspidistra-green felt might be used as a temporary measure.

The soundproofing of the bookshelves could be managed without cost. If we succeeded in getting the librarian to agree, every fifth book could be pulled out so that it overlaps the shelf 3 in. What more natural a baffle system could you devise?

* * *

I have been making one of those simple, well-planned, controlled, and conclusive investigations which everybody is always wanting everyone else to do. The result was unexpected and interesting.

I had taken into consideration all variable factors such as the day-to-day variations in the cycle itself (caked with mud; tyres flat; chain dry and loose), the varying weight of passenger-load (just me; me plus extra jerseys against cold; me with extra equipment—stethoscope, tuning-fork, patella hammer, sandwiches), and the environmental differences (gale force blowing strongly against; rare gale force with; ice or snow; heavy traffic). The result was conclusive—the actual time taken over the journey to hospital by my cycle bore no relation whatever to the expected time.

It was only by chance that I discovered *the* factor determining the speed of my cycle.

Off we went (me and the cycle) on the day of discovery. The morning's punch-card hung to the left of the handlebars, the alarm clock (for accurate timing) to the right. Everything seemed against a rapid journey—the tyres were very flat, a veritable hurricane was blowing against (therefore the cycle was overloaded with me wearing the extra jerseys), and the road was slippery. Cars whipped past splashing mud; we creaked past a milk-van that happened to stop; an old man, at least 80, with a long beard, sitting bolt upright and using the whole of his instep (I was correctly using my toes) on the pedal, streaked past and disappeared into the distance. With resignation we slogged on. A well-shaped pair of bright red nylons twinkled past . . . but then remained just in front. On we sped—sped!—yes: against all previous calculations, my cycle was travelling at tremendous speed just behind the red nylons.

With a brilliant flash of illumination I realised the truth, and further observation has confirmed it. The speed of my cycle is directly proportional to the size and shape of the nylons one cycle ahead.

* * *

I have always had a great deal of sympathy for the village that voted the earth was flat. How dull it is to think that if you keep on walking you will only land up where you started, and how symbolic of our everyday experiences in science, medicine, and politics. Would one not willingly swop this dreary rotundity for an unending vista of flatness, space immeasureable, even though there were a slight risk eventually of falling off the edge? Never having gone all the way round myself to see, I remain an obstinate geoplanarian. I admit the evidence is against me, but I never believe what people tell me anyway. Ships certainly disappear over the horizon, but this is clearly because they get smaller, not because they go over the edge. When they give this impression, it is because they happen to be sinking. The place looks flat enough to me.

So it was cheering news that a rocket sent off by someone or other has proved conclusively that the Earth is not round after all, but pear-shaped, being pointed towards the North Pole. See? They were all wrong! It only remains for further rockets to show that this observation was also wrong, and before we know where we are we shall all be back to pre-Columbian views, and I shall be in the vanguard of the new movement.

* * *

Last Christmas we had occasion to renew our acquaintance with Beatrix Potter. As we opened the pages of the Tale of Pigling Bland out fell a publisher's leaflet inviting us to try reading the Peter Rabbit books in other languages. Some of the titles seem to lose their intimate nursery flavour in the translation: Benjamin Knabbel does not sound at all cuddly, and Peterje Het Konijntje might well be a guided missile. On the other hand, Benda Bynni or Jérémie-Pêche-à-la-Ligne are as euphonious as their originals, and der Hasenfamilie Plumps has a solidity about it which should make die Geschichte well received in Germany.

As might be guessed, I have fallen an easy prey to the publisher's blandishments, and I hope soon to learn more about my old nursery favourite Sophie Canétang and see how her adventures compare with those of Nina Pytt-And or Dili Minllyn.

* * *

Choosing names for infants is difficult, but we are faced with the even more delicate problem of christening two wards set apart for psychiatric patients. Names of famous psychiatrists are frowned on by opponents of their particular school of psychology. Titles like "Ego" and "Id" might lead to strife, and mere numbers or alphabetical letters are too impersonal. Great poets or politicians are regarded as either irrelevant or too psychopathic themselves. To name them after a recent medical superintendent and hospital secretary might be viewed as a rather ambiguous compliment. So far we have reached no solution.

Incidentally, when I came down the stairs after visiting these wards the other day, I observed what seemed to me a charmingly appropriate farewell notice over the exit—"Mind Your Head."

* * *

The sound of the pipes and the savour of haggis at the bicentenary celebrations reminded me that some years ago I treated a patient whose name was also Robert Burns. He claimed descent from an uncle of the bard. Perhaps this fact was responsible for my poetic reaction when his suspected ureteric calculus was shown to be a harmless phlebolith:

Address to a Suspected Ureteric Calculus

Fair fa' your honest sonsie face,
Great chieftain o' the stony race,
Ootside the ureter tak' your place
An' dae nae hairm,
An' ye'll be worthy o' a grace
As lang's my airm.

Invokin' Roentgen's uncan licht
An' viewin' box uncommon bricht
Thro' tissues thick we'll hae a sicht
O' bonny stane
Ootside the ureter—I was richt—
A' on your lane.

Letters to the Editor

MENTAL HEALTH BILL

SIR,—This Bill seems to conceal two major points. The first is the removal of the medical superintendent from the mental hospital.

In the mental hospital the day-by-day circumstances of the patient—food, clothing, heating, lighting, furniture—are as important a part of his regime as physical treatments and psychotherapy. Though the post of medical superintendent is abolished, the work will still have to be done. The chairman of the medical advisory committee lacks the authority of a medical superintendent, and since a large mental hospital needs someone to speak with authority, this responsibility will probably pass to the chairman of the hospital management committee or the hospital secretary. Though they may act from the highest motives, neither is likely to be qualified to make judgments about patients' living conditions. Economy and deference to the opinion of others may obscure the patients' interests.

The second point is perhaps the more important. By some curious chance the freedom of the mentally ill is curtailed by the Bill.

At the moment, the relatives of a certified patient can demand his immediate discharge, and if a debarring certificate is issued it remains in force for 14 days only. If further application is made, it has to be issued once more. According to the Bill, the relatives have to give 3 days' notice of their intention to demand the discharge of a compulsorily detained patient, and, if the doctor intends to issue a debarring certificate, he has these 3 days in which to do so. The debarring certificate lasts for 6 months. If the patient is admitted on an emergency application, his relatives will generally have to wait for 28 days before they can ask for his discharge. At present they have the right to do so at the end of the period for which his short order lasts—usually not more than 3 days with some extensions for a further 14 days. Nowadays a certified patient is automatically discharged if he absconds and remains free for 14 days. It is proposed to increase this to 28 days for the mentally ill and to 6 months for psychopaths.

The provisions made for " guardianship " seem to have escaped attention. So far as the mentally ill are concerned, an entirely new category of patient is created.

An application can be made for any patient with illness of a nature or degree that " makes guardianship suitable " and where it is necessary in his own interests or for the protection of others. Not every medical officer of health will be anxious to have many patients under guardianship, but some may decide that a long list has prestige value and may bring in many elderly eccentric people, perhaps with some trivial mental disability, to swell the numbers. It is perhaps more frightening to realise that a local health authority can apply for a person's guardianship, appoint itself, nominate one of its employees as medical attendant, and reappoint itself year after year.

The local authority also appoints the psychiatrists who are signatories to recommendations for compulsory admission.

Everyone is entitled to draw his own conclusions from the Bill and mine may be wrong. I see the authority within the mental hospitals passing from the doctors to the hospital management committee. Since many problems will lie outside their competence, they will in practice be passed to the permanent lay officials. I see also an increase in the powers of the local authority. Those of us whose experience goes back more than ten years will know that the greatest single cause for the present advancement of psychiatry has been the transfer of mental hospitals from the local authority to the Ministry of Health. I think the greatest care should be taken before a reversal is secured.

De La Pole Hospital, Willerby, E. Yorks. J. A. R. BICKFORD.

CONTROL OF SEPSIS IN MATERNITY HOSPITALS

SIR,—Following a mild staphylococcal outbreak of sepsis in babies in this maternity hospital, consequent on overcrowding, we reviewed our practice in the light of recent articles published in your journal, and well summarised in a leading article.[1]

The conclusions we reached resulted in the following measures:

(1) Avoidance of overcrowding: limitation of admissions by strict control of hospital bookings, and *earlier discharge home.*

(2) Limitation of visitors: one visitor only for the first seven days. Exclusion of infected visitors (severe colds or boils, &c.).

(3) Rooming-in: the infants are to be kept with their mothers. Conversion of large nurseries into lying-in rooms.

(4) Early isolation and barrier nursing by isolation nurses of infected cases and the early transference of infected cases to isolation block.

(5) Isolation on admission of mothers with septic foci (boils, sore throat, vaginal discharge).

(6) Routine nasal swab and high vaginal swab to be taken in all admissions.

(7) Avoidance of the casual use of penicillin. Penicillin should never be used until the antibiotic sensitivity of the infecting organism has been determined. Penicillin should be given only to patients who really need it, and ideally when they are receiving it they should be in an isolated ward, and on discharge the room should be scrubbed down.

(8) *Staff.*—(*a*) All staff (medical, nursing, administrative, and domestic) who have pathogenic nasal swabs should be referred to the E.N.T. specialist for his advice and those passed for duty should use an antibiotic cream (e.g., ' Neobacrin ') in the anterior nares if so advised; (*b*) staff who have any septic lesion (pustules, furuncles, styes, sore throat, coryza, or gastroenteritis) should be examined urgently and possibly placed off duty; (*c*) staff should apply chlorhexidine (' Hibitane ') hand-cream after washing (some hospitals recommend that mothers use it too).

(9) *Infected babies.*—(*a*) infected babies should be isolated, with the mothers, at the earliest possible moment; (*b*) bacteriological swabs (dipped in saline) from the lesion, umbilicus, and the anterior nares should be taken early for sensitivity tests and phage-typing; (*c*) nurses handling infected babies should wear gloves and plastic aprons.

(10) *Babies.*—(*a*) Babies should be bathed in the nursery following delivery and not again until the eighth day; (*b*) dusting-powder containing hexachlorophane (' Ster-Zac ') should be applied to the umbilicus and the surrounding skin, the perineum, buttocks, groins, axillæ, and creases of the neck; (*c*) neobacrin cream should be applied to the anterior nares of the infected infants and their mothers.

(11) Infected rooms should be air-sprayed and the walls, floors, and furniture should be scrubbed down with domiphen (' Bradosol ') 1 in 500. Sheets and napkins and cotton covers should be boiled—sterile binders should be autoclaved. Blankets should be soaked for 24 hours in ' Cirrasol OD ' or domiphen (1 in 1000) before laundering. Screens should be sterilised with steam under pressure. Mattresses should be stoved. In future both mattresses and pillows to be covered with plastic covers, the covers then to be washed with domiphen solution. Better still ' Dunlopillo ' mattresses might prove economical and these could be obtained gradually by replacement.

(12) *Dust.*—Replacement of dry methods for dusting, sweeping, and floor-cleaning in parts of the hospital where patients are exposed, by the use of suction-sweeping attachments and moist cloths. A sweeping-polishing machine should be used. Floor oil.

(13) Soiled linen to be counted and bagged in a hut outside the maternity building.

1. *Lancet*, 1958, ii, 1106.

The local medical officer of health has induced his council to reduce the high charge for home-helps to a very modest one in an effort to popularise home confinement and so help to relieve the heavy pressure on our hospital beds.

We hope these recommendations may prove helpful to other hospitals.

St. Mary's Maternity Hospital, Croydon.

ARTHUR CLIFT
M. SAMSON.

STAPHYLOCOCCAL DISEASE IN HOSPITALS

SIR,—You are to be congratulated on your leading article of Jan. 24, which states the defects of our present system clearly and urges a remedy. I consider a most significant suggestion is the one that someone of sufficient standing in the Ministry of Health should get the Treasury to understand the significance of the report. The National Health Service, though its work cannot be directly measured in productivity, can greatly contribute to the national product if allowed to work efficiently. How many man-hours of production are lost through prolongation of stay in hospital because of wound infection contracted in inadequately ventilated theatres or overcrowded wards?

Pathology Department,
Selly Oak Hospital,
Birmingham.

J. V. GARRETT.

TRACHEOTOMY TODAY

SIR,—It would, I believe, be wrong to let pass without warning the remarks in your annotation (Jan. 17) on the use of tracheotomy and intermittent positive-pressure respiration as a means of transporting cases of simple respiratory poliomyelitis over long distances.

"If, however," you say, "the patient has to be transported over a long distance tracheotomy and intermittent positive-pressure respiration may be necessary, and it has not been shown that these patients suffer any disadvantage compared with their fellows in tank respirators."

In fact the disadvantages of a tracheotomy in a patient with a respiratory paralysis, which is to be partly or wholly permanent, can hardly be exaggerated. Not only does it introduce the complication most feared in these cases—respiratory infection—and thus convert a simple case of respiratory paralysis into a "compound" infected case, but by by-passing laryngeal control of coughing it removes the patient's main means of combating the resulting secretions. A catheter intermittently pushed down the endotracheal tube to suck off these secretions is a very poor substitute indeed for an explosive cough, or even for the "assisted" cough of a patient in a cabinet respirator. The resulting chronic infection which persists (often with acute exacerbations) at least until the stoma is closed—if it can ever be closed—is a severe handicap to the patient with permanent respiratory paralysis. He needs all his lung tissue to be healthy if he is to gain the full benefit of his limited respiratory movement.

Fortunately the R.A.F. have shown us repeatedly that, whatever may be the indications for tracheotomy in respiratory poliomyelitis cases, transport over long distances is not one of them. Both cuirasses and cabinet respirators have been used successfully over long distances, and now that the Tunnicliffe jacket and Emerson bag have been added to the range of apparatus it would indeed be tragic to resort to a method whose consequences can be so calamitous for the patient. In a patient with moderate or severe permanent respiratory paralysis a tracheotomy is a serious complication: at the best it may add six months to a year to his rehabilitation programme; at the worst it can harm his lungs so severely that he remains not only permanently paralysed but chronically ill and permanently in hospital, confined there less by his respiratory poliomyelitis than by his tracheotomy and the attention required for his unhealthy lungs.

Nuffield Orthopædic Centre,
Oxford.

MARGARET AGERHOLM.

IS PEPTIC ULCER AN ENDOCRINE DISEASE?

SIR,—The Zollinger-Ellison syndrome has four main characteristics—gastric hypersecretion and hyperacidity, severe peptic ulceration (often atypical), and a non-insulin-producing islet-cell tumour of the pancreas. The tumours of the pancreas may be multiple, and in the first reported cases the majority were malignant.[1] In some patients adenomas coexist alongside carcinomas; in others there may be an adenomatosis of the gland. In your issue of Jan. 17 Dr. Summerskill described a patient with diffuse hyperplasia of the islet cells, and another patient with islet hyperplasia and one non-β-cell islet adenoma of the pancreas was described at a clinical pathological conference at the Peter Bent Brigham Hospital on Jan. 6, 1958.

The syndrome has naturally emphasised the relationship of the pancreatic pathology and the peptic ulceration. Unfortunately, the ulceration has meant that gastric surgery has accompanied excision of the pancreatic lesion in apparently all patients where excision has been carried out. So far there is no good evidence that removal of the pancreatic tumour alone will affect the gastric secretory function, and efforts to confirm the existence of an "ulcerogenic" pancreatic factor have failed.[2]

Mr. Pender's case (Jan. 17), followed by the letter from Mr. Celestin (Jan. 24), emphasises the incidence of other endocrine disease in these patients—a point also mentioned in your leading article on Jan. 17 which reviewed endocrine causes for peptic ulceration. The article, however, did not mention the fulminating peptic ulceration associated with gastric hypersecretion, which may accompany damage to the hypothalamus in such operations as removal of a craniopharyngioma,[3] a condition very like the Zollinger-Ellison syndrome but without the pancreatic lesion.

Last year a patient, studied at the Massachusetts General Hospital by Dr. W. R. Waddell and his colleagues,[4] had the typical findings of the syndrome except that *no* pancreatic lesion was found at postmortem examination. Dr. Waddell's studies suggested an autonomic dysfunction affecting the blood-supply of the stomach and leading to the gastric hypersecretion and hyperacidity, and this would fit in well with a hypothalamic cause for the syndrome, especially when its common association with other endocrine disease is noted. The hypothalamus has a close relationship with the pituitary gland,[5] and hyperplasia of the thyroid and suprarenals has been frequently recorded with adenomas or apparent hyperfunction of the pituitary; there is also a relationship between the pituitary and pancreatic islet-cell activity, as reviewed by Foa.[6] The hypothalamus provides a pathway from the brain to the endocrine glands, and it has often been noted that a psychological stress has preceded the onset of hyperthyroidism and Cushing's syndrome. Again it was noted that in a group of 10 patients with primary chief-cell hyperplasia of the parathyroid glands recently reported from the Massachusetts General Hospital[7] 5 gave a history of mental upsets. This group also showed other endocrine disease, including a man with a pituitary adenoma and severe peptic ulceration leading

1. Zollinger, R. M., McPherson, R. C. *Amer. J. Surg.* 1958, **95**, 359.
2. Donaldson, R. M., vom Eigen, P. R., Dwight, R. W. *New Engl. J. Med.* 1957, **257**, 965.
3. Dott, N. M. *in* The Hypothalamus: morphological, functional, clinical, and surgical aspects (edited by J. C. Brash); p. 173. Edinburgh, 1938.
4. Waddell, W. R., Leonsins, A. J., Zuidema, G. D. *New Engl. J. Med.* 1959, **260**, 56.
5. Harris, G. W. *Bull. Johns Hopk. Hosp.* 1955, **97**, 358.
6. Foa, P. P. *in* Ciba Foundation Colloquia on Endocrinology; vol. 9, Internal Secretions of the Pancreas, p. 55. London, 1956.
7. Cope, O., Keynes, W. M., Roth, S. I., Castleman, B. *Ann. Surg.* 1958, **148**, 375.

to total gastrectomy but without a pancreatic tumour, his daughter who had two insulin-producing islet-cell adenomas, a woman with severe peptic ulceration (apparently without gastric hypersecretion) and a non-insulin-producing islet-cell adenoma, and two women with suggested hypothalamic disease (gross obesity, tendency to somnolence, and in one a strange menstrual history). It is easy to quote from the literature all permutations of disease in more than one endocrine gland with or without peptic ulceration.

The edifice outlined above for a hypothalamic-endocrine syndrome, with the Zollinger-Ellison syndrome a part of it, can be made attractive, though no doubt as yet easy to destroy in detail. The wider syndrome possibly implies a difference in end-organ (endocrine-gland) sensitivity to a more central stimulus, but this makes pathological sense—hyperplasia leading to adenoma formation leading to carcinoma (perhaps as typified in the variegated pancreatic pathology mentioned in the first paragraph)—especially when the stimulus is long endured and of varied intensity. Certainly there is enough evidence to doubt that the Zollinger-Ellison syndrome is a syndrome on its own. Its chief claim to attention is its emphasis on endocrine disease in patients with peptic ulceration, especially when severe, and the need for search in such patients for endocrine disease.

St. Bartholomew's Hospital, London, E.C.1. W. MILO KEYNES.

TUBERCULOSIS AMONG THE GURKHAS

SIR,—This annotation [1] conveys the impression that chest surgery was made available to patients of the Gurkha tuberculosis sanatorium only when, in 1957, the first patients were transferred to the United Kingdom for lung resection. In fact, thoracoplasties were performed from early 1953 onwards, initiated by Lieut.-Colonel R. M. Johnstone, within four months of his arrival at British Military Hospital, Kinrara. The first were kindly carried out by Mr. A. L. Shields in Malacca General Hospital; and the later operations, after consultation with Prof. D. E. C. Mekie, by Colonel A. J. Clyne at British Military Hospital, Singapore.

London, N.W.8. ANTHONY FAIRBURN.

LUPOID HEPATITIS

SIR,—Although originally applied in error, the various usages of the term "lupus" have become deeply ingrained in medical terminology.

In its earliest form lupus referred to an affliction, not especially of the face as Dr. Anning suggests (Jan. 24), but rather of a limb. In 1396 Lanfrank [2] in his *Science of Cirurgie* mentions lupus in the chapter describing "empostyms", which comprised "eueri swellyng of a lyme, whethir it be greet or smal". Among the empostyms, Lanfrank discusses "another maner passioun that hath diuers names, for summen clepen it cancrum and summen lupum and men of fraunce clepen it malum nostre domine and lumbardis clepen it herisipulam", and it is further characterised by "freting and brennyng and blac colour and stynkynge, and that right foul stynkynge".

Clearly then, if we maintain due respect for the past, we are hardly correct in applying "lupus" to lesions of the face, as in lupus vulgaris and chronic discoid lupus, or to the diffuse disease now known as systemic lupus erythematosus. We believe, however, that advancing knowledge and modern usage has established the process typified as disseminated or systemic lupus erythematosus as something entirely different from that embodied by concepts of the disease current some hundred years ago and earlier. Our employment of the term lupoid hepatitis is an acceptance of this change, unpleasant as it may be to those purists who would have us shackled to antiquity.

IAN R. MACKAY
Melbourne, Australia. D. C. COWLING.

1. *Lancet*, 1958, ii, 1053.
2. Lanfrank. Science of Cirurgie (edited from the Bodleian Ashmole MS by R. V. Fleischhacker). 1396.

TOXÆMIA OF PREGNANCY

SIR,—It is quite evident that both Mr. Scott [1] and Mr. MacGillivray [2] have failed to include cases of mild pre-eclampsia in their statistical analysis, by adopting standards for its recognition that are far too high. It is in the milder manifestations of toxæmia that hydramnios particularly reveals its ætiological significance.[2] Despite this and their failure to assess the response of the myometrium to distension they have both by their data [1 3] incontrovertibly supported the thesis of the uterorenal reflex, as the following comparison of their figures shows (since the incidence of pre-eclamptic toxæmia is about equal in primiparæ and multiparæ in the Liverpool series the figures can be compared with the Aberdeen data derived from primiparæ alone):

	No. of cases		*Incidence of toxæmia*	
	Scott	*MacGillivray*	*Scott*	*MacGillivray*
Unselected	1268	2872	10·7%	24%
With hydramnios	169	123	34% (including 30 cases of gross œdema omitted)	50%
With hydramnios plus further distension (twins, hydrops, diabetes)	21	No comparable figure	52%	..
With hydramnios and *normal* fœtus	100	70	11% approx.	63%
With hydramnios and *abnormal* fœtus	50	53	11% approx.	33%

In both series (line 2) there is a considerably higher incidence of toxæmia when the distension of hydramnios occurs in unselected cases, amounting to doubling in MacGillivray's series and tripling in Scott's if the wrongly omitted 30 cases of gross œdema are included. When to the distending force of hydramnios (line 3) is added the distension of increased fœtal/placental mass in hydrops fœtalis or multiple or diabetic pregnancy, the incidence of toxæmia goes up from 34% to 52%. The Aberdeen figures (line 4) unmistakably support the distension theory; for when, in association with the hydramnios, the fœtus is normal (a preferable ground for comparison in studying the problem of toxæmia) the incidence of toxæmia is $2^1/_2$ times greater than when hydramnios is not present. It is important to recognise that this figure vigorously quarrels with the data collected by Mr. Scott, who reports only an 11% (approximate) incidence in such cases. The probable explanation is the far greater exclusion of the milder pre-eclampsias in the Liverpool series, which largely vitiates the conclusions which are based upon it.

The lower incidence of pre-eclampsia in hydramnios when the fœtus is abnormal without increase in fœtal mass may be due to the lessened blood needs of such an embryo, calling for a diminished blood-flow through the placenta and the myometrium, with a resultant decrease in the turgescence and the resistance to stretch of the uterine muscle. The stimulus of the uterorenal reflex would be thereby reduced.

The placental theory cannot be maintained. Perfectly normal placentas can be associated with pre-eclampsia,

1. Scott, J. S. *J. Obstet. Gynæc. Brit. Emp.* 1958, **65**, 689.
2. MacGillivray, I. *Lancet*, Jan. 3, 1959, p. 51.
3. MacGillivray, I. *J. Obstet. Gynæc. Brit. Emp.* 1958, **65**, 536.

and vice versa. Any placental abnormality does not correspond to the severity of the toxæmia. The recrudescence of eclampsia at labour, days after its subsidence on the death of the fœtus, also rules out placental influence. So does postpartum eclampsia which, though occasionally accounted for otherwise, remains based on the toxæmic process. Even when cerebral hæmorrhage is immediately incriminated in postpartum eclampsia, renal ischæmia has been shown to underlie it [4]—a renal state innocent of endocrine influence yet a proclamation of the uterorenal reflex and its responsibility for toxæmia.

London, W.1. JOHN SOPHIAN.

PANIC AND PHOBIA

SIR,—Experience suggests that the method of treating panic and phobia described last week by Dr. Malleson has a much wider application than he claims for it, though perhaps more in general than in consulting practice.

The professionally isolated life of a G.P. gives him opportunities for looking at problems through glasses untinted with current medical thought, and to me it seems fair to say that the only thing people really fear is the unknown. Once you can break down their problems in terms that they can comprehend and face factually, the element of dread and anxiety is tremendously diminished and frequently abolished, even if you are discussing incurable disease and death (provided you are careful not to raise fresh bogies in doing so by using such words as angina, cancer, or dropsy, which have vast, nebulous, and menacing connotations for many people).

In making a diagnosis of physical disease, we should explain it carefully to the patient in terms of elementary pathology that he can understand and face, without bringing in any emotionally loaded adjectives or nouns. In psychological conditions we naturally cannot do this, but must make our patients explain the diagnosis to us, while we underline for them the essential points in their story as it appears to us. It is no more a kindness in either case to avoid the truth (though we may temper it or approach it obliquely) than it is to avoid inflicting the pain of incising an abscess (though we may use an anæsthetic).

Happiness is what people chiefly want from life, and it is certainly true that a doctor may be a bad one from a scientific standpoint and yet have happy and devoted patients because he can keep at bay the element of fear in their illnesses. But, in the long run, if you are clearing a patch of weeds by hand, the best thing is to recognise the nettles and grasp them firmly.

Kingston-on-Thames, Surrey. CHARLES STEER.

CANCER

SIR,—As honorary secretary of the Cancer Information Association I receive from time to time letters on the relationship between patients and their family doctor in any question of malignant disease. It seems that although the vast majority of the public have complete confidence in their doctors about ordinary illness, there are a large number who distrust them in anything connected with cancer. This unfortunate state of affairs is well illustrated in a letter from a patient recently published in the press. The woman had an innocent neoplasm removed from one breast, but she says "the surgeon's lighthearted dismissal of my inquiries as to whether I might have cancer merely strengthened my belief that I had". For three years she continued to believe that she was being deceived: only when she developed a true carcinoma in the other breast, and had a mastectomy followed by X-ray, did she realise that the first tumour was not malignant. On several occasions the same dissatisfaction with the family doctor concerning cancer has been expressed during "question time" at the end of lectures to women's organisations, and members of the audience have said to me: "You ask us to report symptoms, but I can't talk to my doctor about cancer; I hate being laughed at." Many more complain "the doctors won't tell us anything".

There is no doubt that this tragic state of affairs has been brought about by the hush-hush on the subject imposed by the doctors under the mistaken idea that to talk about cancer to anybody will increase fear, when exactly the opposite is true. There are a great many people who believe they have cancer because the doctor does not realise the importance of being frank with the laity, and many more will not report suspicious symptoms until the tumour becomes a "late stage". In the Registrar General's survey concerning cancer in 1957 the median delay for cancer of the breast is 6·2 months, and 17·3% of all patients suffering from such cancers wait over two years. The delay in some of the other accessible sites is just as bad. If we hope to get a few more early-stage cases, the medical profession must change its attitude to the people about cancer. All patients are not fools.

Cancer Information Association,
337, Woodstock Road,
Oxford. MALCOLM DONALDSON.

NEONATAL HYPERBILIRUBINÆMIA

SIR,—Dr. Timos Valaes (Jan. 24) claims to clarify our paper (Nov. 29). We find his letter confusing and in parts incomprehensible, but he raises some interesting points.

He believes that an exchange transfusion is a "biological experiment" and that knowledge should be gained by close analysis of individual transfusions rather than by relying, as we did, on results from grouped transfusions. The very nature of an exchange transfusion prevents it from being a truly scientific experiment in the sense which Dr. Valaes implies. The basic conditions of the experiment cannot be pre-set or standardised; they inevitably vary from one transfusion to another. Clinical considerations frequently interrupt or necessitate changes in the intended plan; results are subject to the wide natural variability inherent in biological observations; the methods employed are subject to considerable experimental error. Under these circumstances the results of an individual "experiment" must be of only very limited value and must be interpreted with considerable caution. If, however, a sufficient number of observations is made, individual experimental variations are likely to cancel each other out, and the averaged results are likely to yield much more significant information. As we see it, it is the attachment of too much significance to individual results which is the "dangerous attitude"—not our emphasis on broad trends and averages.

Dr. Valaes does not "expect" that our estimated minimum mass will bear a constant relationship to the amount of bilirubin actually removed. We did not rely on theoretical expectations; we measured the relationship. The fact that the estimated minimum mass is always less than the actual amount of bile removed is, of course, of no importance as it is merely being used as a comparative index. It is the variability of its relationship to the actual amount of bile removed which matters. The variability ranged over 24% (58–82%) in a comparison with the estimated output of bilirubin assessed by the presumably more accurate serial-specimen method. Yet when we compared the output as estimated from the actual amount of bile in the waste bottle (the method apparently employed by Dr. Valaes) with the output estimated by the serial-specimen method, we found that there was as much variability between these two "accurate" methods, the variability ranging over 25% (70–95%). The estimated minimum mass thus showed

4. Ehrlich, A., Tyndall, H., Schwarz, J. *Amer. J. Obstet. Gynec.* 1958, **75**, 1189.

itself to be as valid an index of mass of bilirubin removed as other methods.

Dr. Valaes suggests that, before analysis, our results should have been brought to a common basis as far as initial serum-bilirubin level and weight of the baby are concerned. He does not say how this should be done; but presumably he would have us adjust our estimates of mass of bilirubin removed, by proportion, to a common initial serum-bilirubin level and to a common weight. A little consideration will reveal the fallacy of such a manœuvre in respect of initial serum-bilirubin level. We have shown that within the vascular system the serum-bilirubin level is likely to show some variation at different sites. We and others have shown that in an exchange transfusion 50% or more of the bile removed may come from tissues. Does the concentration of bilirubin in plasma bear a constant relationship to concentration in tissues? It almost certainly does not. Because of the time-lag in the passage of bilirubin into tissues a rapid rise in plasma-bilirubin to any given level is likely to be associated with a much lower tissue concentration than would be present had that serum-bilirubin level been sustained for some time. Prematurity and the age of the infant have been shown to modify the relationship between the concentration of bile in plasma and in cerebrospinal fluid.[1] Certain chemical substances are likely to have a similar effect.[2] The fluid shifts which occur in the neonatal period may well also be relevant.[3] As, therefore, there is likely to be such wide variation in the relationship between plasma and tissue bilirubin levels, and as the content of bilirubin in tissues has such an important effect on mass of bilirubin removed, any attempt to standardise results in terms of initial serum-bilirubin levels could well create a far bigger fallacy than it would remove. We are more likely to achieve a common basis by grouping results than by indulging in any such speculative " standardisation " of individual results.

In respect of the weight of the infant, there may indeed be a case for adjusting the amount of bilirubin removed to a common weight. We hesitated to do this, relying rather on a fairly uniform scatter of weights throughout our results. If, however, we had adjusted the mass of bilirubin removed, proportionately to the weight of the infant on the day of transfusion, we should merely have emphasised more strongly the conclusions which we did, in fact, reach regarding the effect of volume and rate of transfusion on the amount of bilirubin removed. The positive correlation between volume of blood transfused and mass of bilirubin removed, and the negative correlation between rate of transfusion and mass of bilirubin removed, would in each case have been stronger. As all the data necessary to make this adjustment were given in our paper, Dr. Valaes could have tested this for himself before suggesting that lack of such adjustment invalidated our results.

In making the statement, " Time is not the only factor controlling the amount of bilirubin that enters the blood from the tissues; a gradient created by the exchange transfusion is also involved ", Dr. Valaes seems to imagine that he is expressing a point of view contrary to ours. If, however, he will study our results he will see that we found that while reduction of rates of transfusion from higher levels down to 0·8 ml. per lb. per min. undoubtedly increased the output of bilirubin, reduction of the rate below 0·8 ml. per lb. per min. did not do so. We did not speculate on the reason for this, but it could be that the critical point of 0·8 ml. per lb. per min. is the point of balance between time and gradient.

Dr. Valaes makes some dogmatic and provocative statements, based apparently on study of " a number of exchange transfusions ". He alludes to his own observations in only a very vague and imprecise way. We hope that he will publish his results in a manner in which they can be adequately assessed and interpreted. There is all too little factual information about the many complex factors involved in neonatal hyperbilirubinæmia.

J. O. FORFAR
A. J. KEAY
W. D. ELLIOTT
R. A. CUMMING.

Edinburgh.

1. Nasralla, M., Gawronska, E., Hsia, D. Y. *Amer. J. Dis. Child.* 1958, **96**, 534.
2. Harris, R. C., Lucey, J. F., MacLean, J. R. *Pediatrics*, 1958, **21**, 875.
3. Gairdner, D., Marks, J., Roscoe, J. D., Brettell, R. O. *Arch. Dis. Childh.* 1958, **33**, 489.

MALNUTRITION IN UGANDA

SIR,—Dr. McFie, in his article of Jan. 10, fails to relate the problem of malnutrition to the many other requirements of an underdeveloped country and thereby does several injustices to those in charge of its public policies and programmes.

Uganda probably produces sufficient food to provide all its inhabitants with an adequate diet if the food were properly distributed and utilised. Ignorance and apathy on the part of the population—not of Government officials—rather than poverty are, in my opinion, the principal factors resulting in malnutrition in Uganda, whatever may be the case in other parts of the world. I think, therefore, that the Uganda Medical Department (of which I am not a member) is correct in placing primary emphasis upon health education as a means of combating malnutrition.

G. W. GALE
Professor of Preventive Medicine,
University College of East Africa.

Makerere College,
Kampala, Uganda.

HUNTING THE NEEDLE

SIR,—The use of an electronic metal locator, such as that described by Berman and Moorhead,[1] has been widely advocated, including a recommendation in your columns by Lambert Rogers [2] for " hunting the needle ". Such an instrument has been in use in this hospital for thirteen years, and many metallic foreign bodies have been removed with its help. A recent case demonstrated its value in an unexpected way.

Half a sewing-needle was run into the hypothenar muscles of the hand of a seamstress. She was admitted to hospital five days later, the foreign body having been displayed radiographically. At operation it was readily localised through the skin with the Berman locator. Exploration was then continued through an incision until it was obvious from the response that the locator probe was extremely close to it. The exposed muscles were then sucked clear of blood preparatory to picking it out.

We then shared the common and frustrating experience of many surgeons in similar circumstances—the needle was nowhere to be seen. To our surprise further probing with the locator produced complete silence in place of the previous confident high-pitched squeal. Our dastardly surmise that the instrument had gone wrong was quickly shamed by its normal response to a metal forceps. It remained for the anæsthetist to suggest, in that quiet, confident way anæsthetists sometimes do, that maybe we had sucked it out. The locator proved him right, finding it easily some way along the suction-tubing, where it lay with point embedded in the wall.

No surgeon will have difficulty in understanding the trouble which the instrument saved the patient, the surgeon, and the X-ray department in this unusual circumstance, and we put the case forward as additional evidence of the value of the locator in dealing with metallic foreign bodies.

Maybe, to forestall possible criticism, we should also note that the use of a tourniquet was purposely avoided in this case, with the consequent need for the sucker.

D. N. MATTHEWS
S. B. OSBORN.

University College Hospital,
London, W.C.1.

1. Berman, S., Moorhead, J. J. Medical Physics (edited by O. Glasser); vol. 2, p. 1102. New York, 1950.
2. Rogers, L. *Lancet*, 1957, ii, 760.

FIBRINATION SYNDROME OF PREGNANCY

SIR,—The detailed hæmatological studies of 4 cases of blood-coagulation failure in obstetrics, reported by Dr. Sharp and his colleagues,[1] are of great value, showing as they do that the trouble is often not merely one of fibrinogen depletion but one in which several of the coagulation factors are involved to a greater or lesser extent. Our experience has been similar, and this is one reason why we have suggested treatment with concentrated plasma rather than with pure fibrinogen[2].

In general the blood findings support the Schneider hypothesis that the train of events is initiated by the intravascular deposition of fibrin consequent upon the liberation of thromboplastin into the general circulation. The only observation which does not fit this hypothesis is that, in certain cases at least, fibrinogen appears to be present but in a state which makes it incapable of conversion into fibrin by thrombin. During recent years we have encountered cases in which blood failed to clot or which showed evidence of only a small amount of fibrinogen when thrombin was added, yet, when treated with calcium and incubated for 24 hours, yielded a normal amount of fibrinogen. Dr. Sharp and his colleagues refer to this phenomenon of what might be called fibrinogen resistance, and we should be grateful to them for any suggestion as to its explanation.

In 2 of the cases which they described, defective coagulation as demonstrated in the laboratory was not accompanied by hæmorrhage. This experience also deserves emphasis.

In 1956[3] we reported the findings in 20 consecutive cases of abruptio placentæ; a gross defect in coagulation was demonstrable in 8, yet in only 2 was there clinical evidence of bleeding. Subsequent studies have confirmed that, whereas coagulation failure is common, it is only rarely accompanied by postpartum hæmorrhage. This shows that the coagulation mechanism is relatively unimportant in the control of bleeding from the placental site when delivery is complete—a well-accepted principle of obstetrics. It may also be noted that women with purpura, or those under the influence of anticoagulant drugs, do not show an increased tendency to placental-site hæmorrhage. We would go so far as to say that, except for bleeding from operative or other wounds in the genital tract, afibrinogenæmia does not directly cause postpartum hæmorrhage. Whether the blood changes can sometimes determine uterine atony (which is the immediate cause of the bleeding) remains to be shown.

Because of such considerations we wish to support the recommendation of Dr. Sharp and his colleagues to the effect that the treatment of individual patients should not be governed by hæmatological findings alone. When a patient suffers from abruptio placentæ it is of some interest to know immediately the clotting powers of the blood; but, irrespective of the findings, treatment should be directed to: (1) encouragement of rapid delivery of the fœtus and the placenta (the source of thromboplastin); (2) rupture of the membranes in the hope of decreasing the transfer of thromboplastin into the maternal circulation; (3) treatment of shock by the usual methods, including restoration of the blood-volume. If obstetric shock is ever attributable to the coagulation upset, it is not caused by fibrinogen depletion but rather by the formation and deposition of fibrin. Any attempt, therefore, to replace fibrinogen while the placenta is still in utero may add fuel to the flames of the fibrination process.

We have now seen 2 patients whose general condition appeared to be made very much worse by infusing a fibrinogen preparation (concentrated plasma in 1 case and pure fibrinogen in the other) while the woman was still undelivered. Our policy now is to withhold fibrinogen until after the end of the third stage. Even at that time there is no need to administer it unless hæmorrhage occurs; the fibrinogen level corrects itself spontaneously in 12–24 hours.

Lastly we welcome the effort of Dr. Sharp and his colleagues to rid us of the unwieldy, unpronounceable and incorrect term "afibrinogenæmia". We suggest, however, that rather than " defibrination " the title " fibrination " syndrome of pregnancy is more correct and simpler. It also has the merit of emphasising the possible danger of giving fibrinogen in the first phase of the disorder.

Department of Obstetrics and Gynæcology, University of Liverpool.

T. N. A. JEFFCOATE
J. S. SCOTT.

1. Sharp A. A., Howie, B., Briggs, R., Methuen, D. T. *Lancet*, 1958, ii, 1309.
2. Scott, J. S. *Brit. med. J.* 1955, ii, 290.
3. Jeffcoate, T. N. A., Scott, J. S. *J. Obstet. Gynæc. India*, 1956, **6**, 266.

PSYCHOTHERAPY IN GENERAL PRACTICE

SIR,—Much is being said and written of the need of doctors in general practice to become better acquainted with psychotherapy, but not much is being done.

The Open Way is therefore expanding its activities to include, besides its full three-year training-course in psychotherapy, a course of seminars specifically for general practitioners, designed to help them to identify, and to know what to do with, those many patients whose ills are not primarily or mainly physical.

The Open Way, which is a charitable trust, is an in vivo experiment in psychological research, taking as its starting-point the axiom that man is by nature spiritual. Any general practitioner to whom this axiom is not anathema will, we feel sure, gain a great deal from these seminars.

Further details will be sent to any general practitioner who will write to the secretary, the Open Way, 37, Queen Anne Street, W.1, or telephone Langham 1941.

The Open Way Psychotherapy Clinic, 37, Queen Anne Street, London, W.1.

ALFRED TORRIE
Medical Director.

POSTMATURITY OR INDUCTION OF LABOUR

SIR,—I was most interested to read the paper by Mr. Theobald (Jan. 10), and to appreciate that attention remains focused on the problem of postmaturity. May I, as one of those quoted in his article, trespass on your space to make a few comments?

Neither my colleagues nor I were able to find any evidence of fœtal hypoxia in cases in which pregnancy was prolonged,[1–3] and I would, therefore, earnestly support Theobald's view that " the fœtus does not live by oxygen alone ". As a corollary, I consider that neither does it die solely from oxygen lack.

I believe that prolonged pregnancy is much more a problem of cephalopelvic disproportion and prolonged labour than of fœtal hypoxia, and, in this connection, the views of Higgins [4] deserve further consideration.

I would support Theobald wholeheartedly, if only because of the social and psychological disturbance of prolonged pregnancy, if I could be satisfied that the duration of pregnancy as calculated was accurate, and that labour followed rapidly on induction and without danger or anxiety. As yet I remain unconvinced on these points in spite of Theobald's persuasiveness, and I am, therefore, unrepentant in maintaining my position.

I think all would agree that the pendulum of opinion on the management of postmaturity has now swung to its full extent in both directions, and for the good of all unborn

1. Bancroft-Livingston, G., Neill, D. W. *J. Obstet. Gynæc. Brit. Emp.* 1957, **64**, 498.
2. Bancroft-Livingston, G., Fisher, O. D. *ibid.* 1958, **65**, 1.
3. Bancroft-Livingston, G., Neill, D. W. *ibid.* p. 4.
4. Bancroft-Livingston, G., Higgins, L. G. *ibid.* 1956, **63**, 567.

infants the sooner the " position of rest " is reached the better. Because of the many conflicting papers written on the subject of placental function in prolonged pregnancy, much fundamental research remains to be done. Theobald's article should provide the stimulus.

Luton Maternity Hospital. G. BANCROFT-LIVINGSTON.

NONCONFORMING NERVE CELLS

SIR,—Since I did not possess Willis's *Compleat Anatomy*, nor the unexpurgated writings of Hughlings Jackson, and being unable to find Dr. Jefferson's (Jan. 10) quotations in *The Anatomy of the Brain* and the bowdlerised Jackson that I did have at my disposal, I remembered Michael Jefferson's powers of parody and realised then the actual function of the redundant cells in the lateral geniculate body of man. They are of course for seeing things that don't exist, and M. J. was using his in the correct manner. And what valuable cells they are, to be sure! Into our pedestrian, earnest world of science they bring the gaiety that is missing from ten thousand out of ten thousand weary dissertations on Fact.

We may go further; for these cells are not connected to anything. They are not bound to the four-dimensional sensory intake that feeds the rest of the mind. Perhaps they are in touch with the dimensionless Universe? Perhaps we should look here for (if one may be pardoned for using a dirty word) the soul? But, no! Our minds return to Earth with a jolt. This is too heavy stuff for these little cells. Prof. Gilbert Ryle wouldn't like it, and neither for that matter would I.

Dr. Menkes' cells (Dec. 27) have to do with fairies, not Ultimates. Magic, certainly, but strictly concerned with our human condition. Yet is not this something worth while? We are exhorted by learned authorities who give us as the fruit of their life's experience that we must work harder, for otherwise we shall become overheavy and die of cardiac infarction. Alternatively they advise us not to lie in bed, or we may lose flesh (and presumably not die of cardiac infarction). What presumption! As scientists we sit smugly on the shoulders of dilettanti who never did work in our sense of the term: who lay in bed till twelve if they felt like it, and preferred to think. When they had conserved enough energy they might get up and write down what they had thought, or dabble with a trial or so at the Royal Society. Now a few cells in our brains have escaped from the Welfare State of universal potboiling, and more power to them. The rest of our brains have never had it so good; and, for me at least, Menkes' strays can have all the metabolites the others get. If they are sports, they seem to be good sports, and probably come in direct line from the genes of some profligate members of a leisured class that no longer exists. We may look forward to the day when no clinico-pathological conference would be complete without someone's asking " And have you looked for L.G. cells? "

But I am sure of one thing. Even in the lateral geniculate bodies of a full-time salaried medical servant, they wouldn't really be part of the N.H.S.

Birmingham, 15. ERIC TURNER.

SIR,—In a world conditioned to conditioning, it is unusual to find Dr. Menkes [1] clinging to the inherent totipotentiality of the neuron without invoking any environmental factor as the agent responsible for the population growth of the lateral geniculate nucleus. Two such powerful external forces come to mind: one of these could support the notion that the 8190 parasitic neurons are non-functioning; whereas the other could support the contention that the neurons actually do function, although perhaps on an unconscious level.

Who of us as we sit before a television set and watch the masterpieces of other non-functioning neurons does not feel that such a deteriorating force is contagious? Teleologically the lateral geniculate nucleus is the first opportunity the brain has of protecting itself against total annihilation. It can do this either by constant depolarisation of the synapse or by outright anatomical cleavage. Dr. Menkes' figures support the latter. As *Homo sapiens* has undergone many mutations to remain alive, so may the ever-increasing non-functioning neurons represent his latest attempts at resisting the television behemoth.

The explanation of Dr. Menkes' findings in terms of still-functioning neurons is far more subtle, as we might anticipate. However, an analysis of the recently developed technique of mass persuasion, " subliminal perception," may shed light on our problem. A clever " motivation researcher " would have polled neurophysiologists and have discovered that the lateral geniculate nucleus stands at the crossroads of the centres of consciousness (midbrain reticular formation) and the centres of visual perception (occipital cortex). What would be more appropriate for commercial needs than to have a group of ever-growing numbers of cells which could respond to the full frequency range of visual stimuli but would only transmit impulses to association centres when stimuli below a specific fusion threshold was received!

The problem, then, still remains which of the two forces is more dominant. Are an increasing number of cells wisely cutting themselves off from television stimuli of eternal duration? Or rather, is " subliminal perception " preempting more and more neurons so that we may never consciously see the brand of cigarette precipitating our early demise?

College of Physicians and Surgeons,
Columbia University,
New York City. STANLEY H. APPEL.

1. Menkes, J. H. *Lancet*, 1958, ii, 1368.

WHAT PRICE STERILISATION?

SIR,—Reading this leading article [1] I was reminded of a happening in an E.M.S. hospital in 1944.

The ward sister was assisting a colleague with dressings. He discarded a pair of used forceps into a tray on the trolley. These were duly picked up by Sister with the aid of a pair of Cheatle's and dropped into the electric steriliser on the trolley. After a moment or two they were picked out, again with forceps, and passed over for further use. Noticing that the steriliser was not connected to any electrical supply the doctor remarked: " But Sister, it's not boiling." " No, Doctor, but it's very deep " was the reply; and it was made in all seriousness.

Natal, South Africa. PHILIP H. DALGLEISH.

TESTICULAR DYSGENESIS

SIR,—You allowed me to protest [2] against Dr. Ferguson-Smith's introduction of the name " primary microrchidism " for this type of female-to-male sex-reversal. Although I recognise gratefully that he has made a concession to Southern tongues by changing the name from "microrchidism" to "micro-orchidism" (Jan. 31, p. 219) I am not moved either by this or by your qualified support of his suggestion (p. 239) to change my mind. Any reason there may have been for the introduction of this unsatisfactory name must surely have now disappeared with Dr. Moore's observation (p. 218) that the testes in the newborn baby with sex-reversal are not small, and Dr. Ferguson-Smith's admission that in prepubertal children they cannot be clinically recognised to be small. Once again, my criticism of his adventures in nomenclature does not abate in any degree my admiration for his patient and rewarding research.

Department of Pædiatrics and Child Health,
Children's Hospital, Birmingham, 16. DOUGLAS HUBBLE.

1. *Lancet*, 1958, ii, 1359.
2. *Lancet*, 1958, i, 1078.

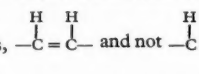
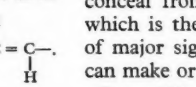
SUPPLY AND DIETARY USE OF FATS

SIR,—Dr. Hugh Sinclair's letters to you are always entertaining, usually provocative, and not infrequently provoking. The one last week, a puzzling mixture of fact and fantasy, is no exception. He has thrown down the gauntlet in such a charming, exhortative, scholarly, but biased manner that I feel obliged to pick it up.

The point of issue arises in the meaning of the term essential fatty acid (E.F.A.).

Even the best-informed readers of *The Lancet* cannot be expected to remember the chemical structures of those acids which most growing animals are unable to synthesise in sufficient quantities for their needs, and which were recognised in the 1930s to be "essential" in the vitamin sense. The deficiency state was first demonstrated in young rats, but it has been duplicated in many other growing animals since, even apparently in babies. The most striking sign of the deficiency state is an unusual dermatitis which Dr. Sinclair and his co-workers have studied over a number of years. But, in addition, the young animal fails to grow or to gain weight at the usual rate, which implies a generalised metabolic disorder. The deficiency state is rapidly reversed when certain fatty acids are fed in rather small doses, and these are called E.F.A.

In recent years Thomasson in Holland and Klenk in Germany have shown that the fatty acids which were effective in remedying this deficiency state have one feature in common: regardless of the number of carbon atoms in the molecule, there were loci of unsaturation (double bonds) between the 9th and 10th, and between the 6th and 7th carbon atoms counted from the terminal or *methyl* end of the chain. (Organic chemists usually number the carbons in fatty acids from the *carboxyl* end of the chain. By contrast, the Thomasson-Klenk nomenclature, which starts at the other end of the chain, speaks of "6 : 9-terminal" double bonds, and so on). Linoleic acid meets this definition (6 : 9-terminal-C_{18}-dienoic acid) as does arachidonic acid (with 20 carbons) with 4 double bonds in the 6 : 9 : 12 : 15-terminal positions. It has also been shown that the hydrogen atoms around these double bonds must be in *cis*

and not in *trans* position, that is,  and not  .

At least six acids are now known to alleviate E.F.A.-deficiency in animals, and all have the *cis*, *cis*-6 : 9-terminal double-bond structure. These orderly studies of an animal deficiency state, which is not recognised in Nature but only artificially produced in the laboratory, led biochemists to the realisation that animals are unable to synthesise enough of these acids of specific structure to satisfy certain metabolic requirements for growth. The exact mechanism of their action remains to be elucidated.

Such, in an oversimplified form, is my understanding of the *classical* definition of an essential fatty acid.

Our report of Jan. 17, to which Dr. Sinclair takes exception, was designed to determine whether dietary E.F.A.s (in the classical sense of the term) were responsible for the lowering of serum-lipid levels which occurs in man when unsaturated fats are fed. I believe our data successfully disprove this possibility, since we found just as great an effect on serum lipids whether corn oil (rich in E.F.A.) or menhaden oil (almost devoid of E.F.A.) was fed. Dr. Sinclair does not pause to explain these observations, made with great care in two metabolically stable patients over a period of many weeks' study, but with religious fervour proposes another definition of E.F.A. This much less strict definition would include all those polyunsaturated fatty acids which cause lowered serum-cholesterol levels in man (but they need have *no* effect on E.F.A.-deficiency in rats!). He theorises that the acids which are thus effective must have some *specific* chemical structure which confers on them this property of influencing human lipid metabolism. Yet, our study proves that corn oil and menhaden oil, which have almost no polyunsaturated acids in common, both lower serum-cholesterol levels. Indeed, the only chemical structural feature which is common to menhaden, corn, whale, sardine, pilchard, cottonseed, linseed, soybean, peanut, safflower, and sunflower oils (all of which cause depressions of serum-lipid levels in man) is polyunsaturation; there is no single acid which is present in roughly equivalent amounts in these many vegetable and marine oils. For these reasons we consider Dr. Sinclair's reshaping of a previously useful term to be misleading and unprofitable.

In conclusion, the *present* evidence indicates that polyunsaturated fatty acids lower serum-lipid levels in man when fed in relatively large amounts, and that this is a non-specific effect of all-*cis*, methylene-interrupted double bonds. We do not know the effect in man of feeding acids of different chain lengths, nor the effect of conjugated double bonds. These questions, and the problem of how the polyunsaturated acids exert their interesting effects on man, remain to be settled by difficult, time-consuming, and expensive experimentation. When Dr. Sinclair designs and accomplishes an experiment which tests whether a diet rich in polyunsaturated fatty acids protects man against the complications of atherosclerosis, we will all look forward with keen anticipation to a factual report of experimental data.

E. H. AHRENS, JR.
Rockefeller Institute, N.Y.C.

EVALUATION OF DRUGS

SIR,—May I correct your report last week on my remarks at the symposium on this subject? One of the points I wished to make was that it is rarely possible to conceal from the nursing staff which is the inert and which is the active preparation in a drug trial. This is of major significance, since the attitude of nursing staff can make or mar trials of this kind.

Banstead Hospital,
Sutton, Surrey. A. A. BAKER.

HEPARIN CLEARING AND PLATELETS

SIR,—On first learning about platelets, who would have imagined that so many important blood factors could be crowded into these tiny granular bodies! At least eight have been described, and now Dr. Mitchell (Jan. 24) is postulating a further addition—an inhibitor of the heparin clearing reaction of lipæmic plasma.

I do not think this is necessary. Dr. Mitchell neglects a platelet effect which he only briefly mentions and which should not be dismissed. This is the anti-heparin action of platelets, which I feel plays an important part in his experiments.

It has been shown that heparin neutralisation is proportional to the number of platelets present.[1] I have found this so in comparing the thrombin clotting-times of heparinised slow-spun (platelet-rich) plasma and a fast-spun (platelet-free) plasma samples. The effect is rapid and persistent after cold storage.

The anti-heparin factor in platelets has been isolated and labelled factor 3 and found to be of clinical significance.[2,3] Its activity is rapid and powerful even in high dilutions. It exists in the phosphatide fraction on platelet extraction and there is no loss of activity after several weeks' storage at 4°C.[4]

1. Canley, C. L., Hartmann, R. C., Lalley, J. S. *J. clin. Invest.* 1950, **29**, 470.
2. van Creveld, S., Paulssen, M. M. P. *Lancet*, 1951, ii, 242.
3. van Creveld, S. *Acta hæmat.* 1954, **12**, 229.
4. van Creveld, S., Paulssen, M. M. P. *Lancet*, 1952, i, 23.

This very stable factor has much in common with Dr. Mitchell's inhibitor factor.

In the platelet-rich plasma samples prepared in his experiments, factor 3 would be readily available to neutralise the heparin in his plasma samples with clearing activity. This effect on heparin would inhibit the appearance of a lipolytic substance, thus slowing the clearance of lipæmic plasma. A lipolytic inhibitor need not be postulated.

I feel that the only important evidence presented which excludes this anti-heparin effect and could support the existence of Dr. Mitchell's factor (i.e., the inhibition of pancreatic lipase) is only briefly and incompletely dealt with and assumes too much to be convincing. Conclusive evidence of the existence of yet another platelet factor must exclude the effects of factor 3 from the experiments. I would therefore suggest that the inhibition of heparin clearing is due to platelet factor 3.

St. Thomas's Hospital Medical School, London, S.E.1. N. G. ROTHNIE.

Parliament

Penal Reform

SINCE the war, though our standards of material property, education, and social welfare have risen, there has been no decrease in the high war-time rate of crime. On the contrary, crime has increased and is still increasing. The white-paper published this week [1] gives the facts about this disquieting situation and sets out some proposals by the Government; but it does not attempt to cover the deep-seated causes which, even were they fully understood, would be largely beyond the reach of Government action.

The main instruments of the war against crime are an efficient police force, the criminal law, and the penal system. The first two are described in the white-paper as the first lines of defence: it is on the penal system that the counter-attack must be mounted. Hence most of the white-paper is concerned with methods of coping with offenders who have been sentenced to some form of detention. It does not discuss other methods of treatment, such as probation.

RESEARCH

Delinquency cannot be dealt with effectively without more knowledge of its causes and a more accurate assessment of the success of various forms of treatment.

The Home Office's new research unit is studying the number of reconvictions of offenders who have been dealt with in different ways. Records are being kept of all boys entering borstal institutions, and they will be studied after discharge so that relevant characteristics can be picked out and related to the likelihood of recidivism. Oxford, Cambridge, and London Universities and the Tavistock Institute of Human Relations are studying such forms of treatment as probation, prison, detention, and attendance centres, and the psychological and sociological process of groups of men brought together under prison conditions. A large-scale study of crimes of violence against the person is being made in London by Cambridge University.

A start has thus been made with intensive studies; but the area is large and ill defined and at present there is no agency outside the Home Office which can keep the whole of it under critical review. The white-paper welcomes the proposal to set up an institute of criminology at Cambridge.

PENAL METHODS

Penal methods have developed piecemeal and need periodic revision. As crime is related to the pattern and outlook of the society in which it occurs, so penal methods may need to be adapted to the society in which they operate. Modern criminal law has almost lost sight of the concept of personal reparation which was the basis of early law; indeed in the public mind the interests of the offender may sometimes seem to be placed before those of his victim. Perhaps our penal system would be a more effective deterrent, and have greater moral value, if the concept of reparation were added to those of punishment and reform. This change could not be separated from a reconsideration of the prisoner's level of earning. The principle put forward by the late Margery Fry, that the obligation to the victim rests primarily on the society which has failed to protect him, would entail a scheme of Government compensation. It presents practical difficulties, but a working party is to examine it.

YOUNG PEOPLE

The Ingleby Committee, set up in 1956, are reviewing the treatment of children and young people, and the Government will await their report before considering how to deal with those who come before juvenile courts.

The striking increase in crimes by young adults emphasises the need for a review of the penal treatment of this group. The system is at present overstrained. Detention centres are full; young people may wait 12 weeks in a local prison before a vacancy can be found at a borstal; many young prisoners have had to serve the whole of their sentence in a local prison. The Prison Commissioners urge the provision of more detention centres so that all sentences of 6 months or less may be detention and not imprisonment. To take the place of sentences of over 6 months and under 3 years, they propose a single indeterminate sentence of custodial training with a maximum of 2 years, within which the offender may be released at any time after 6 months.

ADULTS

The system of imprisonment for adults has been handicapped by the rising prison population, overcrowding, shortage of staff, and insufficient capital expenditure. But two new forms of treatment have been introduced—corrective training and preventive detention. The basis of classification has been revised, and new types of prisons started. Evening education, pre-release courses, and aftercare have all been extended. It is easy to imprison a man (the white-paper suggests): the difficult thing is to release him.

We still do not know how well the prisons serve their purpose of sending the prisoners out "better men and women, physically and morally, than when they came in". In 1957 some 87% of men and 89% of women of the star class had not returned after 3 years "outside". But the proportion of prisoners with five or six previous offences has slowly increased over the past 5 years. There is no reason to believe that an increasingly repressive regime would have a better effect on these recidivists than humane and constructive methods. The deterrent effect of imprisonment must finally lie in the loss of personal liberty.

The local prisons are grossly overcrowded: some 6000 men in them are sleeping three in a single cell without adequate facilities for work or training. They are being asked to perform too many specialist functions for which they are not equipped—e.g., examination of untried prisoners, classification of the convicted, training of offenders serving substantial sentences. Proper observation and classification centres should be built, near the remand centres for young people, so that they can use the same diagnostic staff.

There should be enough work to keep a prisoner busy for a full day and a full week. In the central and regional training prisons this ideal has been largely fulfilled, but in local prisons the position is deteriorating. The problem will never be solved until society accepts that prisons do not work in an economic vacuum and that prisoners are members of the working community, temporarily segregated.

Acceptance of this view would lead to reassessment of the principles on which prisoners are paid: the present rate is about 2*s*. 8*d*. a week. If they were paid at normal rates and had to find money for their board and keep, social-insurance contributions, and savings, it would make for self-respect, greater

1. H.M. Stationery Office. Cmnd. 645. 1959. Pp. 32. 2*s*. 6*d*.

interest in the work, and greater security on release. But would such a system really help to train a prisoner when so much of his income would be deducted compulsorily? What would its moral effect be unless it were linked with a system of restitution to the victim?

PRISON PSYCHIATRY

Since the war psychiatric clinics have been set up at Wormwood Scrubs, Wakefield, and Holloway. Work will be starting shortly on a psychiatric prison hospital. When it is ready the major psychotherapy carried out at the clinics will be concentrated there. But psychiatrically experienced doctors can do much to help disturbed prisoners and should be available in larger prisons. Unfortunately there is a lack of qualified candidates for these posts, and prison doctors have to spend the greater part of their time on work for the courts.

The white-paper ends with a minimum building programme. This will take both money and time, and even if it were completed today there would still be 1500 men sleeping three in a cell in local prisons. The most hopeful and quickest way of relieving congestion, it is suggested, would be to place more men in open prisons.

In introducing the white-paper Mr. R. A. BUTLER, the Home Secretary, announced the appointment of a Working Party to consider compensation of victims of crimes of violence, and of a standing committee on the revision of criminal law.

Princess Louise Hospital for Children

LAST June the Minister of Health agreed to allow St. Mary's Hospital to convert 39 out of 76 beds at the Princess Louise Hospital for temporary use as maternity beds during the reconstruction of St. Mary's own maternity unit. The Minister deferred his decision on St. Mary's second proposal—ultimately to convert the whole of the children's hospital for adult use. Both these proposals have aroused opposition and were discussed in the House of Lords in 1957.[1] On Jan. 28 Lord BALFOUR of BURLEIGH brought forward a motion asking the Minister to reconsider his decision and to see whether St. Mary's needs could not be met by converting other children's beds in older hospitals. He suggested that it was only St. Mary's possession of the Princess Louise that had prevented the regional board years ago from converting their less efficient children's beds to adult use, and that the admitted shortage of adult beds and surplus of children's beds in the area had not been adjusted because responsibility was divided between the regional board and the teaching hospital. He believed that the Minister could have taken action to set this matter right.

Lord Balfour pointed out that attendances at the Princess Louise had risen steadily to 1700 inpatients and 30,000 outpatient attendances in 1957. Last year the hospital had coped successfully with an outbreak of bronchiolitis where 104 infants were admitted to the hospital within a matter of weeks. The Minister had said that he recognised the merit of special children's hospitals, but his present decision would close a large efficient unit and scatter the children over the face of the Earth.

Lord MORAN opposed the motion on the ground that, if hospital beds were no longer necessary for the purpose for which they were originally designed, they must be set free by the Minister for purposes which the community required. In all branches of medicine the days of small hospitals were numbered. To get first-rate accessory departments the pædiatric unit must be big enough to supply them itself (like Great Ormond Street) or it must be a block attached to a general department which had these departments.

The Earl of ONSLOW said that he had been authorised by the Minister of Health to say that he was not prepared to direct the North West Metropolitan Regional Board to convert children's beds in their hospitals to meet St. Mary's need, but, if at this eleventh hour the two boards could agree on an alternative proposition, he would willingly consider it.

1. See *Lancet*, 1957, ii, 41; *ibid.* 1958, ii, 199.

Lord COTTESLOE (chairman of the North West Metropolitan Regional Board) said that the need for maternity beds in the area was urgent in 1957. Owing to a growing population it was now far more urgent. Eighteen months ago the Minister had asked his board if they would accept the Princess Louise as a children's hospital. With some reluctance but with a desire to be helpful, the board had said that they would and had offered to make available to St. Mary's (though without full administrative control) 50 beds at St. Charles' Hospital. St. Mary's had been unable to accept this offer. But the situation had changed, and he thought that if the same question were put to his board now they would not be prepared to renew their earlier offer, for it would mean some temporary small reduction in the number of maternity beds, which would aggravate the already serious maternity position.

Lord AMULREE thought it a pity to shut down the Princess Louise because it was the newest and most modern place for the treatment of children in that part of London. Lord TAYLOR pointed out that one of the most important medical reasons for introducing the National Health Service was to enable us to deploy our forces at the point of greatest need. Hospitals must be flexible and adaptable.

Lord COHEN of BIRKENHEAD said that he was immensely conscious of the need to retain voluntary service with the hospital service. The hospital boards and committees were all statutory instruments of voluntary service. Local good will, which was not a statutory requirement, must also be retained, and anything that disturbed the good will of the public in our hospitals should be avoided, but the need to secure a balanced service was an overriding factor. Before the National Health Service we had no hospital system, and in his view Lord Balfour's motion would perpetuate the laisser-faire policy of the past, allowing everyone to try to hold on to his own without considering the needs of the community as a whole. He put the number of beds which the Princess Louise needed to accommodate its average number of inpatients at 46, which meant that there was a surplus of 30 beds there. Within two miles, there were six other hospitals providing over 200 beds. St. Mary's home-nursing scheme, which was a new venture, had already made it unnecessary for 500 children to go into hospital.

The Earl of DUNDEE, replying for the Government, said that during 1957 only 36 beds on average were occupied at Princess Louise's throughout the year. Having regard to the acute problem of finding services to deal with maternity cases, he did not see what other course the Minister could have taken than to approve St. Mary's suggestion for the two years during which the reconstruction of their maternity department would put 29 beds out of action. On the long-term question of what should happen to the Princess Louise after these two years, he thought it undesirable to make any forecast. We could not foresee what the needs of the community or what the feelings of the staff of the Princess Louise would be in two years' time.

The motion was lost by 47 votes to 14.

More Babies, Fewer Midwives

IN the course of an adjournment debate on Jan. 26, Mr. HORACE KING drew attention to the shortage of midwives. In the ten years of the National Health Service the number of midwives had fallen only slightly, from 17,095 to 17,006, but there never had been enough midwives and, as in the same years the number of births had risen by $1^1/_4$ million, a bad position had become worse He gave the following examples of hospital boards and local authorities which were having difficulty in filling vacant posts:

Sheffield Regional Hospital Board, out of sixty-three maternity units, had eleven with a 50% deficiency and twenty-six with a 20% deficiency. In 1957–58 they had to close three units. Southampton had two vacancies for midwives which had been advertised for 3 months without a single applicant. Portsmouth advertised a vacancy for a year and had only one applicant. A new maternity unit had been completed at Spalding last May. In November the local Press had reported that it could not be opened because there were no midwives.

Midwives, he continued, were supposed to have 36 hours a week off duty and 5 weeks' holiday a year. In fact, they rarely got 2 consecutive nights off call. They got their holidays only by other midwives undertaking double districts during their absence, and when they returned from holiday they returned to do a double duty to enable some other midwife to have a holiday. The profession claimed that a midwife ought to attend a maximum of 55 cases a year singlehanded or 66 with a pupil midwife; yet in Southampton seventeen domiciliary midwives delivered in 1957 an average of 92 babies per midwife. In other parts of the country the position was worse.

Hospital maternity units were also overworked. The number of hospital confinements rose from 395,000 in 1955 to 428,000 in 1957. If the hospital nurses' working week was to be reduced from fifty-six hours to forty-four hours, 3000 extra hospital midwives would be needed.

QUESTION TIME

Microbiological Warfare

Mr. EMRYS HUGHES asked the Minister of Supply what personnel he employed at the Microbiological Research Centre and Chemical Defence Experimental Establishment at Salisbury Plain and for what purpose.—Mr. AUBREY JONES: It would not be in the public interest to give the figures asked for. The Ministry of Supply Establishments at Porton are mainly engaged in carrying out research on defensive problems of microbiological and chemical warfare. The researches are essentially directed towards assessing the threat and providing defences against it. The large majority of the results obtained are published in open scientific literature. The threats include the botulinus toxin referred to in recent newspaper statements. This substance has been well known for many years and the threat posed is grossly exaggerated, since the toxin cannot be easily disseminated and is not self-propagating. A number of useful defensive measures are in fact known against it. It is possible that other bacteria or viruses spell a greater danger, and the purpose of my Establishments at Porton is to determine and reduce these risks—a task in which in some respects they have been notably successful.

Mr. EMRYS HUGHES: Has the Minister's attention been directed to the speech made last week by Sir Robert Watson-Watt in Montreal in which he says that this establishment has invented a substance, 1 lb. of which could wipe out the whole world? Does he not expect a little public interest in this? Can he tell us if any of these scientists are employed in the manufacture of typhus, cholera, and polio germs; and if this is purely defensive, why is it not handed over to the Minister of Health?—Mr. JONES: I think that my answer indicated some acquaintance with the speech made in Montreal the other day by Sir Robert Watson-Watt. As a matter of fact, his statement is clearly akin to the one made as long ago as 1946. It is included in a book published in 1950 to exactly the same effect. As to the purpose of the establishments, I can only repeat—and it has always been the policy of this country—that their purpose is almost entirely defensive.

Mr. P. NOEL-BAKER: Has the Minister seen the observations of Major-General Brock Chisholm of Canada about the great dangers of the policy of secrecy concerning biological warfare, and will he consider whether he cannot give the public more information about this most dangerous development in the means of war?—Mr. JONES: It is quite an old development. I have seen the remarks made by Dr. Chisholm and, as I said in my main answer, most of the results deduced from researches made at Porton are, in fact, published in open scientific literature. Indeed, the present director at the Porton establishment is in India giving a lecture on means of combating plague.

Dr. EDITH SUMMERSKILL: How can the Minister reconcile his first statement with what Dr. Chisholm has only recently stated.—Mr. JONES: Because I do not accept everything that Dr. Chisholm says. Indeed, as I think was apparent in my first main answer, I think that most of what has been said both by Dr. Chisholm and Sir Robert Watson-Watt has been grossly, indeed ludicrously, exaggerated.

Obituary

MATTHEW FELL

K.C.B., C.M.G., F.R.C.S.

Lieut.-General Sir Matthew Fell, director of the Royal Air Force Medical Branch from 1918 to 1921, and director-general of Army Medical Services from 1926 to 1929, died at Barrow-in-Furness on Jan. 28, at the age of 86.

A Lancashire man, he was educated at Sedbergh and St. Bartholomew's Hospital, qualifying in 1898. The following year he joined the R.A.M.C. and served in the South African War, being awarded the Queen's medal with four clasps and the King's medal with two clasps. Between 1902 and 1905 he served with the South African Constabulary, thereafter returning to this country.

In the 1914–18 war he went to France as staff officer to the director of medical services, B.E.F., and was subsequently an A.D.M.S. in the Third Army. From France he went to Mesopotamia, where he was largely instrumental in reorganising the medical services. He was eight times mentioned in despatches, and was appointed C.M.G. in 1917, C.B. in 1919, and K.C.B. in 1922. At the time of his appointment, in 1918, as director of the R.A.F. Medical Branch, the Royal Air Force had just been established as a separate entity; and in the two years that he held office he established the Medical Branch on firm foundations. Accordingly when he returned to the Army in 1921, his reputation was much enhanced. Five further years in the Army Medical Services were followed in 1926 by his appointment as their director-general. To this task he brought the energy and originality which had marked his tenure of the R.A.F. directorship; but, through no fault of his, the Army Medical Services were falling on lean days owing to economy measures. He retired in 1929 and went to live in Lancashire.

A colleague recalls meeting him in Constantinople in the 1914–18 war:

"Matthew Fell loved to talk in the mess after dinner and we sat at his feet and took it all in. He talked well, and at this long distance I still remember with pleasure the accounts he gave us of his life in South Africa after the Boer war. They were vivid stories and he made it sound very attractive. He was kind to young officers, but expected a good deal from them, and when he knew he was getting this he would support them very loyally when help was needed."

H. E. W. writes:

"My most vivid memories of Sir Matthew Fell are of when he was in his prime. He was a born leader of men, a first-class administrator, firm and popular with the executive as well as his professional colleagues, and blessed with the gift of judging quickly the ability and character of people.

"I first met Fell early in 1916 when he was a colonel in the R.A.M.C. en route to Mesopotamia to take up the post of A.D.M.S. There was a large contingent of R.A.M.C. on board the ship, most of them having joined temporarily for the war. Throughout the voyage, Fell made a particular point of getting to know each officer and other rank. Many of them he met again in the field during the Mesopotamian campaign, and they were surprised and most gratified to find that he recognised them. In fact, he had a habit of following up the career of those who served under him and whenever possible of furthering their interests. He endeavoured to fit the pegs in the right holes. This characteristic did much to raise morale and the standard of work. This was never more necessary than it was in Mesopotamia in 1916 after the defeat at Kut when the medical services were severely criticised. There were few regular medical officers in Mesopotamia; the majority of the temporary ones had practically no training before going overseas, and the forces generally were unseasoned. The result in the field was chaos. More than 40% of the forces either

died or were invalided each month and the majority of those remaining were sick with dysentery, malaria, or heat effects. The D.M.S. was frequently ill, so the brunt of the reorganisation rested on Fell's broad shoulders. By dint of his personality, initiative, and drive the whole picture was changed within the few hot months' respite (shade temperatures 110–120°F) before the projected advance at the end of the hot season. By this time, owing largely to Fell's leadership, the medical services were adequately equipped and provided for and morale was high, and in the advance the medical services won their laurels.

"I was next privileged to serve under Sir Matthew in the Royal Air Force when he became its first director of medical services in 1919. He was seconded from the R.A.M.C. for this purpose, his task being to inaugurate and build up a separate medical service for the R.A.F. to deal in particular with the special problems of aviation medicine. After three years he left the Air Ministry having firmly established the medical services on sound principles, which have stood the test of time, including acid testing during world war II. Even in retirement Fell maintained contact with those who had served with him in the R.A.F. and took a great interest in all modern developments. He was the father of the R.A.F. Medical Service, and he expressed his great joy of living to witness the fruition of his plans and the important part played by that service in world war II. The Royal Army Medical Corps and the R.A.F. Medical Service have lost an outstanding leader and friend in the passing of Sir Matthew Fell."

Sir Matthew Fell married in 1908 Marion Isobel, daughter of Robert Wallace, and had two sons and two daughters.

WILLIAM HENRY FRANCIS OXLEY

M.R.C.S., F.R.C.O.G.

SOME twenty years ago Dr. Oxley was one of the most notable doctors in the East End of London. He ran a large general practice in Poplar, he was a pioneer in industrial medicine and toxicology, and his work as obstetrician drew consultants from all over the world to the East End Maternity Hospital in the Commercial Road to study his effective, if unorthodox, methods.

After he qualified from Barts in 1897 he started in practice in the East India Dock Road, and soon he added to the work of his practice appointments, such as that of surgeon dispenser to the Seamen's Hospital, certifying factory surgeon, and obstetrical surgeon to the Nursing Home of St. John the Divine, which were to point the way to his future work and interests. After some years he moved his practice to the Manor House, Poplar.

In the 'twenties he became medical officer and lecturer in midwifery at what was then called the East End Mothers' Home. The low maternal mortality which he achieved there claimed the attention and respect of obstetricians. The hospital, which had been started in the early years of the century, was an important school of midwifery, and it was staffed by midwives who called in the general practitioners of the neighbourhood. It was an early centre of pioneer antenatal work, and in 1929 at a meeting of the British Medical Association Dr. Oxley was able to report that among the last 10,000 confinements there had only been one slight fit and that there had been no maternal death from placenta prævia among the last 14,000 cases. Though by the 'thirties he was in charge of a large midwifery service, he remained a general practitioner at heart. He challenged the official findings of the day, which tended to put much of the responsibility for the high maternal mortality on the family doctor.

Dr. Oxley was himself a valued, if perhaps militant, member of the maternal-mortality committee of 1928–32, and he was chairman of the clinical subcommittee. He had been one of the foundation members of the College of Obstetricians and Gynæcologists, and in 1931 he was elected F.R.C.O.G. in recognition of his work for this committee.

A colleague writes:

"Oxley was a man who was supremely self-confident. He was prepared to undertake any vaginal obstetric operation with his matron, Miss Anderson, as anæsthetist. His results around 1930 were extraordinary, and his maternal mortality for years must have been the lowest in the world. Leading obstetricians from other countries visited his ramshackle hospital consisting of a row of old Georgian houses. He claimed that the reason for his success was that he had no house-surgeon, that all obstetric treatment was carried out by himself, and that his patients were almost all pure cockneys who did not suffer from small pelves. His methods were unorthodox; he had no sterile dressings, no gowns, no masks, and no gloves. His only antiseptic was perchloride of mercury, and he sutured the perineum with silver wire.

"I last saw him about the end of the war, on A 5 near Dunstable. His hospital had been evacuated to Northamptonshire, while he remained in Poplar, but he used to visit the hospital regularly. He must have been nearly 70 and was still full of fire."

Dr. Oxley died on Jan. 28 at the age of 82.

NOAH PINES

M.B. Kiev, L.M.S.S.A., D.O.

Dr. Noah Pines died at his home in London on Jan. 10 at the age of 71.

He was born in Moscow, and, after qualifying at Kiev in 1911, he became assistant to his uncle, Leon Pines, a distinguished ophthalmologist in Warsaw. During the 1914–18 war he served with the Russian cavalry and received high decorations. After the Revolution he and his family escaped to Belgium. He came to England in 1920, and took an English qualification the same year. As his command of English was poor he answered his papers in Latin, which was one of his many scholarly attainments. He settled in the East End of London, where he soon acquired a large practice, but he did not give up his ophthalmic interests. For many years he was registrar in the eye department of the London Jewish Hospital, and he carried the whole of the departmental responsibilities during the late war. During this period he was an indefatigable worker for the St. John Ambulance Brigade, and throughout the heavy bombing in Stepney he never failed to visit shelter after shelter, attending to the wounded. For his devotion to duty and bravery he was decorated with the Order of St. John of Jerusalem. In the midst of his other duties he continued to find time for research, and his published work included papers on the retinopathies. He was a frequent contributor at clinical meetings.

H. G. and G. K. write:

"Noe Pines had infinite curiosity: before he believed anything he had to test it and find out for himself. After he retired from practice at the age of 70 he became interested in the electron microscope, and only a week before he died he discussed its development at a meeting of the Royal Society of Medicine, keeping his angina in check with nitroglycerin.

"As a practitioner he had, perhaps, a too easy belief in therapies, but in consultation he rarely needed the help that he sought. He had a Puckish personality and was quick in movement and thought. He never spared himself and had a deep understanding of his patients. He was a deeply cultured man, well versed in history and with an enormous memory. He was loyal to the Jewish tradition, and he was interested in all developments in Israel and in all Jewish cultural movements."

Dr. Pines' widow, daughter, and two sons are all doctors.

Notes and News

SUPPLEMENTARY ESTIMATES

THE supplementary estimate for the National Health Service in the current financial year [1] shows an increase for England, Wales, and Scotland of £18,966,206, bringing the total net cost to £549,678,636. Of the additional sum, £9,272,000 goes to hospital boards to provide for increases in remuneration and other costs and accelerated maintenance work and replacement of equipment; £2,435,000 goes to the general medical services for increased payments to general practitioners; and £2,842,000 goes to the pharmaceutical services.

W.H.O. EXECUTIVE BOARD

CONTINUING its session which opened in Geneva on Jan. 20,[2] the W.H.O. Executive Board unanimously endorsed a programme for extended medical research, presented by Dr. M. G. Candau, the director-general. Dr. Candau observed that, great as any national research effort may be, there remain problems which cannot be solved within national boundaries. Some require exploration in particular geographic areas or climatic conditions, among populations of different races, or in particular conditions of living. His report described six categories of research problems particularly suitable for international collaboration:

1. Those of world-wide significance, such as the genetic description of populations and the measuring of the incidence and prevalence of disease. Certain other problems, while not world-wide, require study on a region-wide basis (e.g., kwashiorkor and others common to all tropical countries).
2. Communicable diseases: tuberculosis and many virus diseases that are universal, and malaria, which requires a regional approach.
3. Cancer, coronary thrombosis, hypertension, rheumatoid arthritis, and diabetes mellitus, in which comparison of health and illness in different environments and economic conditions may provide the key to understanding. Dr. Candau urged speedy exploration of these contrasts, which tend to disappear with rapid social change and evolution.
4. Rare conditions which may have general practical importance. For instance, study of the pulmonary hypertension reported in populations living above 4000 metres may throw light on pulmonary hypertension in general.
5. A fifth category arises from the need to assist highly skilled research-workers to combine their experience for the expeditious solution of problems.
6. Lastly, there is a need for international cooperation because the necessary research resources are lacking in some countries where problems are found.

The Board discussed plans for a new building to house the headquarters of W.H.O. in Geneva. A move to a separate building has become necessary because present accommodation in the Palais des Nations is insufficient for present or future W.H.O. operations, and because the other organisations working in the Palais are also in critical need of additional office space. Some members suggested that the possibility of the headquarters being located outside Switzerland should also be considered; but it was pointed out that such a decision could be taken only by the World Health Assembly. The Assembly will consider the proposal to build new headquarters at its session opening in Geneva on May 12.

THE OTHER HOSPITALS

IN April, 1957, a new method of departmental costing was introduced in some 200 large hospitals, each with an annual expenditure of at least £150,000. This replaced the earlier simple system of cost analysis by which all expenditure was arranged under general headings, such as salaries and wages, and fuel. The earlier system provided a figure for the average cost of maintaining a patient in hospital but did not readily show the cost of the different departments and services. The first figures for the 200 hospitals were published last October.[3] It is planned to introduce the new costing arrangements by stages; and the remaining hospitals of the National Health Service in England and Wales continued to use an improved version of the old system, which, though not as elaborate as the new scheme, provides unit costs for some departments. The second volume of Hospital Costing Returns [4] gives the figures for these hospitals for 1957–58.

The catering cost per person fed per week in a chronic hospital is £1 9*s.*, in a maternity hospital £2 2*s.* 11*d.*, in a mental-deficiency hospital £1 3*s.* 10*d.*, and in a children's hospital £2 0*s.* 3*d.* The report also includes some national average costs for all hospitals (including the 200 large hospitals). In 1957–58 the net inpatient cost per week was £33 4*s.* 2*d.* for a London teaching hospital (£29 9*s.* 5*d.* in 1956–57), £19 5*s.* 10*d.* for an acute hospital (£17 17*s.* 8*d.* in 1956–57), and £6 2*s.* 1*d.* for a mental-deficiency hospital (£5 10*s.* 6*d.* in 1956–57).

N.H.S. SUPERANNUATION SCHEMES

WHEN the National Health Service was started in 1948 contributory superannuation schemes were set up for England and Wales and for Scotland. The statutory regulations provide for accounts to be kept by the Health Departments of all revenue and expenditure under the schemes, and notional interest on the mean balances is credited to these accounts at rates determined by the Treasury, the rate being 2½% per annum up to March 31, 1955, and 3¼% thereafter. The regulations further require actuarial investigations to be made in 1955, and at seven-yearly intervals thereafter, to determine what adjustments are needed to maintain a balance between the assets and liabilities of each scheme. In his report on the Civil Appropriation Accounts [5] for 1957–58 the Comptroller and Auditor General states that at March 31, 1955, the schemes showed actuarial deficiencies of £80 million for England and Wales and £6 million for Scotland, equivalent to some 15% and 9% respectively of the total liabilities of the schemes.

The deficiencies are attributed partly to liabilities imposed upon the schemes at their inception, but the main single factor has been the increase in the general level of salaries since 1948. This is estimated by the Government Actuary to be responsible for about half the deficiency in England and Wales and about three-quarters of the deficiency in Scotland. In assessing the deficiencies the Government Actuary took account of pay increases made in 1955 but assumed that pay scales would be stable thereafter. There were, however, further pay increases in 1956 and 1957, and if allowance had been made for these increases the actuarial deficiencies would have been approximately £105 million for England and Wales and £8½ million for Scotland. Discussions have been taking place with the Treasury on the action to be taken on the Government Actuary's reports.

University of Oxford

On Jan. 22 the degree of B.M. was conferred on the following:

Jack Dodd (in absentia); L. M. McEwen, M. A. Rucklidge.

University of Cambridge

On Jan. 24 the following degrees were conferred:

M.B., B.Chir.—G. D. Blackledge, *R. W. Sherwin, *N. A. Subedar.

M.B.—John Blake, *P. H. T. Greig, *J. M. L. Jones, *W. T. Menke, M. J. Raphael, *David Rhys-Phillips, R. M. Simons, J. W. Soper, J. R. Strong.

* By proxy.

University of Manchester

The following appointments have been made:

Dr. J. N. Mills, reader in physiology; Dr. N. W. Preston, senior lecturer in bacteriology; Dr. S. B. de C. Baker and Dr. Goldwyn Sclare, lecturers in pathology; Dr. J. F. Watkins and Dr. Roy Postlethwaite, lecturers in bacteriology; Dr. Bryan Corrin, assistant lecturer in pathology.

World Health Day

Each year the World Health Organisation sponsors World Health Day on April 7. Mental Illness and Mental Health in the World of Today has been chosen as the theme for 1959.

1. 1958–59: Supplementary Estimates and Estimates for Revenue Departments. H.M. Stationery Office. Pp. 154. 8*s.*
2. See *Lancet*, Jan. 31, 1959, p. 263.
3. See *Lancet*, 1958, ii, 1319.
4. National Health Service. Hospital Costing Returns: Year Ended March 31, 1958. Vol. II: hospitals which operated the alternative scheme. H.M. Stationery Office. £1 10*s.*
5. H.M. Stationery Office. 1959. Pp. 345. 19*s.* 6*d.*

Royal College of Physicians of London

At the comitia of the college held on Jan. 29, with Dr. Robert Platt, the president, in the chair, the following, having satisfied the censors' board, were elected to the membership:

Harvey Baker, M.B. Leeds, P. K. M. Barrett, M.B. Lond., E. M. P. Brett, B.M. Oxon., D. A. Chamberlain, M.B. Cantab., R. C. Curran, M.D. Glasg., Kenneth Davison, M.B. Durh., D. A. M. Ellis, M.B. Lond., Pamela M. Fullerton, B.M. Oxon., J. B. L. Gee, B.M. Oxon., R. U. Gillan, M.B. Birm., E. N. Glick, M.B. Leeds, C. J. Good, B.M. Oxon., C. B. Grieve-Dingwall, M.F. N.Z., J. B. Gurland, M.B. Cape Town, Courtney Hodgson, M.B. Birm., R. O. H. Irvine, M.D. N.Z., A. MacL. Kingon, M.B.E., M.B. Lond., J. P. Knowles, M.B. Cantab., P. M. Last, M.B. Adelaide, D. R. K. Medley, B.M. Oxon., George Michell, M.B. Sydney, D. C. F. Muir, M.B. Lond., W. R. Murdoch, M.B. Glasg., G. R. Osborn, M.B. Melb., P. J. Preston, N. B. Pride, M.B. Cantab., R. C. Richards, M.B. Durh., R. P. G. Rothwell, M.B. N.Z., A. L. Sanderson, M.B. Lond., J. M. Small, M.B. Lond., J. H. Swallow, M.B. Cantab., I. L. Thompson, M.B. Sydney, C. Chai Soon Toh, M.B. Sydney, J. B. Tucker, M.B. Lond., A. N. Turnbull, M.B. N.Z., Arumakuttige Parakrama Jayasena Weerasekera, M.B. Ceylon, A. J. P. Willis, M.B. Lond.

Licences to practise were conferred on the following who have passed the final examination of the Conjoint Board:

Abigail Esi Etruba Amua-Sekyi, M. A. McL. Bailey, R. B. Barnbrook, E. J. Barnett, P. J. Beale, L. J. Beilin, B. A. O. Binns, Balideo Bisseru, R. M. Bradfield, J. S. Brown, Doreen R. G. Browne, J. C. Bull, A. E. Bullock, Jill A. Bunton, Hazel M. Burtenshaw, W. G. Cheyne, Katharine L. Codd, Ann R. Coe, J. A. Corbett, H. S. Cormack, A. M. Cotton, Barbara A. Croft, E. G. L. Davies, T. T. Davies, Richard de Alarcon, P. J. De Buse, Avery S. Denfield, Harvey Dexter, B. W. M. Dorran, D. L. Easty, D. Obidinma Ekwulugo, Ephraim Udofia Essien, Valerie J. Everett, Monica J. Falkner, Samir Elias Farraj, Shirley Fish, W. E. I. Forsythe-Jauch, A. L. Freeman, Louise Gallagher, Sheila M. Gorringe, T. R. Gould, A. E. Green, P. R. Grob, Anne A. N. Grubb, J. M. Gurney, Henry Haberfeld, A. P. Hall, C. E. Harley, Rosemary Harms, John Harrower, B. A. Hasenson, M. T. Haslam, Elizabeth A. Hills, H. B. Holden, J. G. Holmes-Smith, William Holms, Rita J. Hornik, C. Anyaegbunam Ifeakandu, Gillian A. Jefferies, Ann P. John, D. W. McN. Johnson, D. G. H. Jones, Shirley P. Jones, Arshalouis Kasbarian, B. N. C. Kempton, R. L. King, F. W. Knox, Setlur Narasimha Iyengar Krishnaswamy, Jean M. Kubale, K. L. Lancer, D. W. Laurie, P. A. Lawrence, R. D. B. Leicester, P. K. Lewin, M. J. Lewis, T. P. Linehan, Tee Fun Loh, Cynthia Lucas, I. S. Macdonald, Hazel J. McFarlane, Anne M. MacGregor, C. McL. Maddox, Valerie Major, Napier Malcolm, Ann C. Martindale, D. D. Mathews, R. W. May, H. J. Missen, B. D. G. Morgan, P. A. Morris, M. K. Murphy, T. G. Nash, Ruth Ogden, Bak Chua Oh, T. Chukwunyere Okeahialam, Theophilus Adewale Oleghe, J. T. Outred, Ann Parry-Williams, Ronald Paul, D. K. Payler, P. E. Pearce, W. B. Pearce, M. G. Peters, Audrey E. Pett, A. D. Piatkus, E. C. Pye, C. A. Ramsay, M. I. Reeve, Jennie Robertson, T. W. E. Robinson, M. D. Robson, J. W. Rollins, G. C. Rowe, Helen Rubens, S. S. Sanders, Martin Sarner, Margaret L. Shaw, D. J. Smith, J. H. Sowray, A. J. Spicer, June M. Squire, M. I. L. Stolar, T. C. Taylor, I. R. Thomas, A. F. Tredre, Athasit Vejjajiva, A. L. Whiteson, C. E. R. Winer, John Wolfle, William Yen, June R. Zagni.

The following diplomas and those mentioned in our issue of Jan. 17 (p. 157), were conferred jointly with the Royal College of Surgeons:

D.C.H.—T. P. Linehan, Kathiravaloo Tharmarajah.
D.I.H.—A. J. Barwood, Anand Bhoomkar, J. L. Blonstein, T. N. N. Brennan, D. C. Curtin, B. R. Ellis, J. G. Jeffs, D. L. MacKinnon, Satyaranjan Ray, T. H. Redfern, Ziyauddin Qamaruddin Shaikh, J. J. Slome, Lakhmir Singh Sodhy.
D.M.R.T.—J. N. Godlee.
D.T.M. & H.—Muhammad Abdul Jalil Khan.

On Thursday, Feb. 19, at 5 P.M. at the college, Pall Mall East, S.W.1, Dr. Peter Kerley will give the Marc Daniels lecture. His subject will be mass radiography in the prevention of disease—a survey of 400,000 boys aged 18.

Royal College of Obstetricians and Gynæcologists

At the meeting of council held on Jan. 31, with Prof. A. M. Claye, the president, in the chair, the following were elected to the membership:

Ernest Aldous-Ball, K. R. Barnes, S. L. Barron, Kamala Bose, J. A. C. Brown, Enid M. Carey, Kalyani Chatterjee, Ki-Kit Chow, Sydney Cohen, K. V. Cooper, Mohini Dass, G. M. Davidson, B. H. Dawson, Suryamoni Devi, Rita D. Dickinson, Piyatissa Dissanayake, P. M. Elliott, R. G. Emerson, B. N. Foy, R. D. Fraser, Aloka Gupta, Irene C. Hain, J. J. Handler, Shaukat Haroon, J. G. Harrington, Sakti Ram Hazra, Michael Howett, R. F. Hutchings, Hugo McVey, Bimla Mehta, J. J. Morrissey, Harold Mukheiber, Ivan Orr, R. J. Ostolosky, J. F. O'Sullivan, Keki Dinshaw Printer, M. A. Pugh, Saroja Ramaswamy, Ann L. Reynolds, Jayatissa Nalin Rodrigo, Malti Rohatgi, Rita W. Shannon, G. R. Sharp, D. H. Stewart, W. Siang Hwa Tow, Margaret A. Wignall.

Society of Apothecaries of London

At recent examinations the following were successful:

M.M.S.A.—M. T. C. Mower.
L.M.S.S.A.—J. S. H. Tooth, J. G. Perry, J-P. C. M. Brookes, S. A. Vanar, M. P. Sternberg, M. C. Gabriel, A. H. Y. Lee, D. G. Sargant, M. L. Woods, C. R. Sulochana, M. J. Croxson, A. E. T. Smith, D. I. Fry, W. A. Rosser.
D.I.H.—A. L. Cairns, D. C. Curtin, D. L. De Sousa, P. J. Fahey, J. S. E Gilbart, D. S. Jani, C. R. May, P. Oliver, D. M. Williamson.

International Hospital Congress

The International Hospital Federation will hold their congress in Edinburgh from June 1 to 6. Further particulars may be had from Captain J. E. Stone, 6th Floor, 34, King Street, London, E.C.2.

North of England Obstetrical and Gynæcological Society

The following officers have been elected for 1959:

President, Mr. H. Agar; vice-presidents, Mr. D. W. Currie, Mr. S. B. Herd, Dr. E. A. Gerrard, Mr. T. G. Robinson, Miss D. C. Bates; hon. treasurer, Mr. T. B. FitzGerald; hon. general secretary, Mr. J. B. Farquhar; hon. reporting secretary, Miss U. M. Lister.

College of General Practitioners

Upjohn travelling fellowships.—Applications are invited for not less than fifteen travelling fellowships (£200 each).

They are open to members of the college who wish to spend at least two weeks in postgraduate study at their old teaching hospitals or at any other hospitals, clinics, health centres, or general practices of their choice in the United Kingdom or Eire. They are not available for study overseas. Application forms may be had from the secretary of the college, 41, Cadogan Gardens, London, S.W.3, and should be returned before Aug. 1.

Lady Tata Memorial Trust

The trustees invite applications for grants, scholarships, or fellowships for research on blood diseases, with special reference to leukæmia.

Programmes of research on any aspect of malignant disease which may throw light on problems of leukæmia will be considered, and awards made to investigators of any nationality, working in any country where payment can be made. Particulars and application forms may be had from the secretary of the (European) scientific advisory committee of the Trust, Chester Beatty Research Institute, Fulham Road, London, S.W.3. Applications must be submitted before March 31.

Society for General Microbiology

This society will hold its general meeting from April 6 to 8 at the Senate House, University of London, W.C.1. The meeting will include a symposium on virus growth and variation on April 7 and 8. On Tuesday, April 7, at 5.30 P.M. Dr. G. S. Wilson will give a Marjory Stephenson lecture. The subject will be faults and fallacies in microbiology. Further particulars may be had from the general office of the society, c/o Institute of Biology, 41, Queen's Gate, S.W.7.

Training Posts in Hospital Administration

Applications for a further 16 training posts for prospective hospital administrators are invited.

The posts are open both to young officers already employed in the National Health Service and to graduates and professionally qualified people who wish to make hospital administration their career. Further particulars may be had from the Ministry of Health, Savile Row, London, W.1.

National Association for Mental Health

This Association will hold its annual conference at Church House, London, S.W.1, on March 19 and 20. The subject for discussion will be the place of work in the treatment of mental disorder. Further particulars may be had from the conference secretary, 39, Queen Anne Street, W.1.

Hospital Organisation and Methods Service

The Ministry of Health has now put its experimental organisation and methods service on a permanent basis (H.M. [59] 13). Any regional board which wishes to do so may appoint an additional officer (at the grade of assistant secretary) to specialise in O. & M. and work study activities.

Deaf Children

Since deaf children should begin their auditory training as early as possible, the London County Council has decided to admit them while they are still under 5 to day nurseries for two hours a day, so that they may mix with normal-speaking children. The staff will give them special attention by talking to them. The hearing of children of deaf parents is often retarded, because their opportunities for talking are restricted, and they, too, will be eligible to enter the nurseries at an early age. For both groups of children there will be no charge for admission.

Faculty of Radiologists

This faculty will hold a postgraduate course on March 21 and 22, at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2. Further particulars may be had from the secretary of the faculty, 47, Lincoln's Inn Fields, W.C.2.

Royal Medico-Psychological Association

An examination for the Gaskell gold medal and prize (£75) will be held in May. Particulars may be had from the secretary of the Association, 11, Chandos Street, London, W.1.

Medical Art Society

This society will hold its annual exhibition from Feb. 5 to 25 (daily from 10 A.M. to 5 P.M., and on Saturday from 10 A.M. to 1 P.M.) at Walker's Galleries, 118, New Bond Street, London, W.1. Admission is free.

A clinicopathological conference on the carotid artery syndrome will be held at Westminster Hospital Medical School, Horseferry Road, London, S.W.1, on Thursday, Feb. 12, at 5.30 P.M.

The North of England Otolaryngological Society will hold a meeting in Middlesbrough on Saturday, Feb. 21, at 2 P.M.

The Biochemical Society will hold a symposium, on the biosynthesis and secretion of adrenocortical steroids, on Saturday, Feb. 14, at 10.30 A.M. at the Senate House, University of London, W.C.1.

Dr. Frederick Wolff has been appointed assistant professor of medicine at Johns Hopkins Hospital, Baltimore.

A plaque has been placed at the gates of Hartley House, Plymouth, to commemorate the birth there, on Jan. 18, 1868, of Sir Leonard Rogers. Sir Leonard now lives in Falmouth.

An informal dinner was held in London on Jan. 23 in honour of Dr. W. Mayer-Gross on the occasion of his 70th birthday. It was organised by Prof. Martin Roth and Prof. Erwin Stengel with about 40 of Dr. Mayer-Gross's past and present colleagues and pupils.

A semipermanent exhibition is being held from Feb. 2 to 25 at the Institute of Dermatology, Lisle Street, London, W.C.2, on keratoses and bullous lesions affecting oral mucosa.

The C.M.F./M.E.F. Physicians' Reunion Dinner will take place at the Rembrandt Rooms, London, S.W.7, on Saturday, March 21. The hon. secretary is Dr. A. Willcox, 59, Harley Street, W.1.

CORRIGENDUM: *Gastric Hypersecretion.*—In this letter last week (p. 258) Dr. J. L. C. Dall's initials appeared incorrectly.

Appointments

BEARE, R. L. B., M.B. Lond., F.R.C.S.: part-time consultant in plastic surgery, St. Mary's Hospital, London.

DRUMMOND, JAMES, M.B. Edin., D.P.H.: district M.O.H., Chesterton, South Cambridgeshire, and Newmarket, and deputy county M.O. and deputy principal school M.O., Cambridgeshire.

KELLY, T. S.-B., M.B. Manc., F.R.C.S.E., D.O.M.S.: consultant ophthalmic surgeon, Bath clinical area.

Hertfordshire County Council:

BARNARD, MILDRED M. E., M.B. Lond., D.P.H.: assistant M.O.

HARBORD, K. W. M., M.B. Dubl.: assistant M.O.

WILKES, ANNA, M.B. Durh., D.P.H.: assistant M.O.

Sheffield Regional Hospital Board:

BROWN, D. E., M.B. Lond., F.F.A. R.C.S., D.A.: consultant anæsthetist, Thoracic Unit, Leicester Isolation Hospital, and Chest Unit, Leicester.

FINNEGAN, T. R. L., M.D. Lond., M.R.C.P.: part-time consultant physician, Derby area hospitals.

GURLING, K. J., M.D. Lond., M.R.C.P.: part-time consultant physician, Derby area hospitals.

Western Regional Hospital Board, Scotland:

BROWN, F. O., M.B. Glasg., F.R.F.P.S., D.M.R.D.: assistant radiologist, Stirling and Falkirk area.

CAMERON, J. A., M.B. Glasg.: senior assistant to area-supervising tuberculosis physician, Dumfries and Galloway area, and deputy physician-superintendent, Lochmaben Sanatorium.

GRAHAM, A. J., M.B. Aberd., D.P.M.: assistant psychiatrist and deputy physician-superintendent, Woodilee Mental Hospital, Lenzie.

MILLER, J. H., M.B. Glasg., F.R.C.S.E.: assistant orthopædic surgeon based at Royal Infirmary, Glasgow.

MUTCH, JOHN, M.B. Lond., F.R.C.S.: assistant orthopædic surgeon, Falkirk and District Royal Infirmary.

ROY, A. D., M.B. Glasg., F.R.C.S.: consultant surgeon, Western Infirmary, Glasgow.

WILSON, GEORGE, M.B. Glasg., D.A.: assistant anæsthetist, Ballochmyle Hospital, Mauchline, Ayrshire.

Diary of the Week

FEB. 8 TO 14

Monday, 9th

UNIVERSITY COLLEGE, Gower Street, W.C.1
5 P.M. Prof. Alexander Haddow: The Chemistry and Biology of Cancer: 1. History—Experimental Carcinogenesis. (First of three lectures.)

GUY'S HOSPITAL, London Bridge, S.E.1
5.15 P.M. Dr. P. M. F. Bishop, Dr. Ian Somerville: Hirsutism.

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
4 P.M. Prof. M. L. Rosenheim: Unilateral Renal Disease and Hypertension.

UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Mr. I. M. Stewart: Bone Replacement.

Tuesday, 10th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
3.45 P.M. Dr. F. C. Chesterman: Hetero-transplantation of Human Tumours and Tissues. (Imperial Cancer Research Fund lecture.)

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine and Therapeutics.* Dr. J. P. Shillingford, Dr. Lawson McDonald, Dr. Percy Cliffe: Indicator Dilution Curves in Heart Disease.
8 P.M. *Psychiatry.* Prof. Martin Roth, Dr. Arthur King, Dr. J. C. Little: Phobic Anxiety-depersonalisation Syndrome.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. J. M. Walshe: Biochemical Studies in Hepatic Coma.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. Dr. Erica Wachtel: Use of Vaginal Cytology in Gynæcology.

ROYAL ARMY MEDICAL COLLEGE, Millbank, S.W.1
5 P.M. Brigadier F. A. R. Stammers: Delayed Complications of Partial Gastrectomy.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. P. D. Samman: Diseases of the Nails. (Second of two lectures.)

BIRMINGHAM MEDICAL INSTITUTE, 36, Harborne Road, Edgbaston
8 P.M. *Psychiatry.* Dr. D. T. Maclay: Boys Who Commit Sexual Offences.

MANCHESTER MEDICAL SOCIETY
8 P.M. (Clinical Sciences Building, York Place.) *Surgery.* Mr. Arnold Ashworth: Partial Nephrectomy. Mr. Thomas Moore: Bladder Neck Obstruction in the Female. Mr. D. S. Poole-Wilson: The Use of the Ileum as an External Urinary Conduit.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Dundee.) Dr. P. B. Marshall: Bio-assay Methods in Clinical Research and Diagnosis.

Wednesday, 11th

POSTGRADUATE MEDICAL SCHOOL
2 P.M. Dr. I. Friedmann: Aural, Nasal, and Vocal Cord Polypi.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Mr. O. S. Tubbs: Surgical Treatment of Mitral Valve Disease.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. I. B. Sneddon: Bullous Eruptions.

MANCHESTER MEDICAL SOCIETY
5 P.M. (Medical School, University of Manchester.) *Pathology.* Dr. C. H. Adderley: Clinical Pathology—A Survey. (Presidential address.)

UNIVERSITY OF ST. ANDREWS
4 P.M. (Department of Medicine, Dundee.) Dr. F. L. Mitchell, Prof. R. B. Hunter: Methods of Investigation of Adrenal Cortical Function.

Thursday, 12th

ROYAL SOCIETY OF MEDICINE
5 P.M. *Ophthalmology.* Mr. K. C. Wybar, Miss C. Douthwaite: Place of the After-image Treatment in Amblyopia.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Dr. Paul Fatt: Synaptic Excitation and Inhibition in the Central Nervous System.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Cytodiagnosis in Dermatology.

ALFRED ADLER MEDICAL SOCIETY
8.15 P.M. (1, Wimpole Street, W.1.) Dr. E. Weissman: Dynamics and Structure of Personality.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Mr. Rowland Osborne, Dr. W. Burston, Dr. Rodney Green: Modern Aspects of the Treatment of Cleft Lip and Palate.

UNIVERSITY OF ST. ANDREWS
5 P.M. (Physiology Department, Dundee.) Dr. P. B. Beeson (New Haven): Pathogenesis of Pyelonephritis.

Friday, 13th

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. F. P. Raper: Pelvi-ureteric Obstruction.
4 P.M. Prof. N. H. Robson (Adelaide): Myeloproliferative Syndromes, Variants of Leukæmia.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Mr. J. W. Cope: Diagnostic Problems Involved in Vertigo.

MIDLAND CENTRE FOR NEUROSURGERY, Holly Lane, Smethwick
8 P.M. Prof. Norman Dott: Surgical Disorders of the Pituitary Region.

PLYMOUTH MEDICAL SOCIETY
8.30 P.M. (Freedom Fields.) Prof. R. A. Willis: Experiments on Tissue Transplantation.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH, Edinburgh, 8
3.30 P.M. Mr. A. I. S. Macpherson: Late Results of Splenectomy.